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HIDROSADENITIS AXILLARIS OF VERNEUIL

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Hidrosadenitis of the axillary glands was probably first described by Velpeau, who called it "abcès tubéreux de l'aisselle. The name "hydrosadénite phlegmoneuse" was given it by Verneuil in 1864. He had described it previously, as had Richet, Nélaton and Chassaignac.

The disease is not uncommon, and it presents a definite clinical picture, but it is apparently not very well known, probably because it is hardly mentioned in most works on surgery in the English language, and is not mentioned, or is only briefly described, in many of the text-books on dermatology.

This paper summarizes what I have been able to find on the subject in the medical literature. It is incomplete because I have been disappointed in having seen no cases of hidrosadenitis since I discovered that so few and so inconclusive studies have been made on the question of its origin in the sweat glands.

Hidrosadenitis is found most frequently in the axillae, but it is occasionally seen about the anus, in the areolae, and on the scrotum and labia majora. This discussion is confined to hidrosadenitis of the axillae, as that is the only location in which I have seen it. I have seen it only in women, but it occasionally occurs in men.

CLINICAL APPEARANCE

It is unusual to see the development of the disease from its start as it gives little trouble at first. The course of development of new lesions, however, makes clear the usual sequence of events. One or two or more hard nodules, rarely larger than a pea, are felt accidentally in the axilla. An increasing number of nodules, with some discomfort, brings the patient to the physician. By this time there are usually half a dozen or more nodules. Verneuil's description of the progress and appearance of the disease will serve as well as later ones.

At first: slight mobile subcutaneous induration, rolling under the skin and between the fingers; spontaneous pain and pain on light pressure; very little or no elevation; no appreciable redness. This lasts three or four days. Then the tumor begins to get larger; it advances to the skin which in its turn is inflamed and becomes adherent; a slight redness is seen and pressure becomes painful.

† Dr. Lane died Oct. 17, 1933.

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Some spontaneous pains appear and are exaggerated by movement of the arm. The tumor is still very hard; no sign of fluctuation is found; there is only glandular swelling; resolution is still possible, and is not very rare.

But suppuration often follows; the elevation increases in size; the skin becomes thinner and turns a dusky red; the epidermis begins to exfoliate. In the center of the induration a softer spot is seen. The redness extends somewhat. Pain is sometimes sufficiently sharp to restrain the mobility of the arm, and the difficulty of lifting it from the side of the body makes observation difficult.

Fluctuation is difficult to obtain because of the small quantity of fluid accumulated. . . .

If incisions with the point of a lancet are made at the top of the elevations a few drops of thick, viscous pus come out, escaping in the shape of a flat, coherent ribbon, like the semiliquid contents of the collapsible tubes of paint used by artists. Immediate relief follows this little operation. A few hours, or at most, a day later, suppuration has stopped, and only a few drops of viscous serum are with difficulty seen running out. The redness in the center and at the edges fades out. But the induration seems hardly affected by this evacuation. It begins to resolve only after two or three days, and as it subsides, follows the same course as during its period of growth; that is to say, it detaches itself from the skin and becomes free in the subcutaneous tissue, where it may be perceived for a long time—ten, fifteen, twenty days and even longer.

This is the usual course of events. If the condition is neglected there is usually spontaneous rupture through the skin. Verneuil reported cases in which rupture was not external but into the loose tissue of the axilla, forming large abscesses there. As noted by Verneuil, the evolution of each nodule takes about two weeks, but as new ones keep appearing the process may extend over several months.

LOCATION OF ABSCESSES IN SWEAT GLANDS

Verneuil made no histologic studies in his cases, and in 1854, when he suggested that the sweat glands were the site of the abscesses, he said: "I make this observation only with reservations, for it is chiefly the curious distribution of these collections that made me adopt the interpretation which I give here. It is therefore a point to be restudied and to be demonstrated in a more satisfactory manner." In his later papers he seemed convinced that the location of the abscesses was in the sweat glands.

There have been few histologic studies of hidrosadenitis, and the results do not agree sufficiently to settle the question of the origin of the abscesses in the sweat glands.

Török, who made some studies in 1902, concluded: "Perhaps I gained the impression that the pathological process indeed is located chiefly in that layer of the skin which incloses the glomeruli of the sweat glands but that from the beginning it is in no wise connected (*gebunden*) with the sweat glands."

These results were practically confirmed by Talke in 1903 and by Rost in 1922. They found the epithelium of the sweat glands normal

in the early stages, and only in the later stages of the inflammation were the glands infiltrated with pus cells. Rost proposed the theory that the infection was carried by the lymph channels and that it affected first the interstitial tissue and secondarily the stroma of the glands.

In 1924, Rutz came to the opposite conclusion. He stated:

> Our microscopic investigations gave the following clear findings. In early cases we found the epithelium of the sweat glands infiltrated with leukocytes, the glandular epithelium broken down and in process of desquamation. The lumen was free. The interstitial tissue around the sweat glands was entirely free of leukocytes, and the subcutaneous tissue and the sebaceous glands were not touched by the infection.
>
> In late cases the sweat gland still remained in the center of the inflammatory process. . . . We always found a group of sweat glands closely filled with leukocytes, with diffuse infiltration of the periglandular tissue.
>
> The infiltration gradually became less dense as the distance from the glands became greater. The ducts were sometimes free but, for the most part, were filled with polymorphonuclear leukocytes.
>
> Whether the infiltration was an inflammatory reaction in the periglandular tissue or pus breaking through the thin wall of the gland is hard to say. We, however, incline to the latter opinion.
>
> *But in all cases, we believe that the beginning of the inflammation is in the sweat gland itself.*

Gans' studies led him to the conclusion that the invasion of the sweat glands follows infection of the interstitial connective tissue and of the lymph channels.

An interesting point which seems to be more than a coincidence is the fact that hidrosadenitis occurs only in the regions of the body in which apocrine glands are found. The apocrine glands, to which this name was given by Schiefferdecker in 1922, are a variety of sweat glands differentiated from the other sweat glands (eccrine glands) by their morphology, secretion, development and incidence. They arise from the primary epithelial germ in association with the hair follicle, as do the sebaceous glands, but from a different part of the epidermis. Their secretion contains cytoplasm plus secretory products, and there is a clearcut cycle of secretion. In man these glands are found in the axilla, around the nipple and the pubis, labia majora and scrotum.

Dr. Harold S. Burr, Professor of Anatomy in the School of Medicine of Yale University, has given me assistance in the interpretation of Schiefferdecker's findings and hopes to carry on further investigations of these glands and, when the opportunity arises, of the question of the origin of hidrosadenitis in them.

In this connection, it may be mentioned that Darier is of the opinion that Fox-Fordyce disease, formerly considered a variety of prurigo nodularis, should be classed as a disorder of the sweat glands. He gave the following reasons:

> It is almost entirely confined to the female sex; . . . is essentially regional; is found in the axillae, on the pubis and labia majora, in the perineum, around

the nipples and sometimes near the umbilicus; in a word, in the locations where apocrine glands are found. . . .

At first this disease appeared to most authors, and still appears to some, to be a variety of *neurodermite*. As in *neurodermite*, histologic examination shows acanthosis, hyperkeratosis and periglandular and perivascular infiltration. But in addition there is found marked, sometimes cystic, dilatation of the apocrine glands.

ETIOLOGY

The location in which hidrosadenitis occurs is favorable for infection. The lesions have the clinical appearance of staphylococcic infection, and though I have found no detailed study of that question, the statements that have come to my notice are that the staphylococcus is usually found.

It is not surprising that the sympathetic nervous system has been invoked as a contributing etiologic factor. Rutz expressed the belief that the infection "is favored by a constitutional component sympathicotonia."

DIAGNOSIS

The appearance and course of development of hidrosadenitis are so typical that there is no difficulty in recognizing it. The common furuncles or larger abscesses are much more painful and deeper and usually do not occur in large numbers; when they are opened there is a plentiful discharge of pus, followed by a later slough of necrotic tissue. With hidrosadenitis there is usually little or no fever.

Only a word need be said as to the confusion of names. The clinical description of hidrosadenitis as given by Verneuil was so similar to that of some of the tuberculids that at first they were considered varieties of hidrosadenitis. This led Pollitzer to give the name "hydradenitis destruens suppurativa" to the lesions now called papulonecrotic tuberculids. In like manner, Dubreuil called them "hydradénites suppuratives disséminées." At about the same time Barthélemy gave the name "acnitis" to similar lesions. As these tuberculids are now well recognized and occur in totally different regions, the names alone are confusing.

TREATMENT

Many treatments have been suggested. Vaccines or foreign proteins seem to have given no favorable results.

In thirty-one cases in various stages Rutz obtained good results with roentgen therapy, which he recommended in all stages of the disease. Peyser said that this method may be tried and that it is useful in early cases but that it is not always successful. Of course, ultraviolet radiation has been recommended, and also bacteriophage.

In the usual case my custom has been to keep hot compresses on the axillae part of the time and to incise the pustules when evidence of

pus is seen, or earlier if necessary to relieve the discomfort caused by tension. In one case under my observation, which was seen early, the condition subsided with no formation of abscesses following the use of hot compresses for several days. The induration was palpable for between two and three months before it finally disappeared.

In stubborn cases of long duration with continued relapses, it may be necessary to excise the skin of the affected area. In a few such cases, Dr. W. F. Verdi has obtained good results by making an incision through the center of the affected area, turning back the skin, curetting out the nodules from below the surface and keeping the wound packed with gauze as long as necessary. Klug has used a similar procedure.

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EXCRETION OF BISMUTH IN A SERIES OF CLINICAL BISMUTH TREATMENTS

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The clinical efficiency of treatment with bismuth compounds in syphilis has been sufficiently demonstrated by all the available methods—by the clinical progress, by the disappearance of spirochetes from the lesions and by the reversal of the Wassermann reaction. However, these methods are not sufficiently sensitive to distinguish sharply the optimal conditions for the use of this treatment, such as the concentration and duration that may be required and the relative efficiency of different preparations. This limitation of clinical experience is reflected in the multiplicity of preparations, dosages and instructions for spacing of injections. It may be presumed that compounds which differ in solubility differ also in rapidity of absorption, and therefore of excretion, and in promptness and duration of action. If continued action is essential, as seems probable, too rapid absorption would necessitate frequent injections and very slow absorption would not only delay the effect but tend to produce cumulation and toxicity. It is therefore, desirable to study the course of bismuth through the body by quantitative methods. The absorption from the site of the injection may be judged by the thinning of the roentgen shadow, but this is of limited accuracy. Chemical analysis of the local tissues of animals killed at various periods after injection gives comparable data, but the anatomic conditions and the dosage are different from those observed in the clinic. Much more useful information can be obtained from patients. The most pertinent item is the concentration of bismuth in the blood plasma, but it is not feasible

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to secure samples adequate for analysis sufficiently frequently. However, since the intensity of the excretion of bismuth is determined chiefly by the concentration in the plasma, the urinary excretion especially is a fair index of the actively circulating bismuth, and this is probably the effective bismuth, for, as with mercury, the action seems to cease promptly after the administration is discontinued, when there are still considerable amounts of bismuth fixed in the tissues. A number of studies of clinical excretion have been published, the most extensive by Mehrtens, Hanzlik and their co-workers. The plan of the present inquiry differs in that a number of patients, generally at least three, were used for each condition studied, so as to obtain the normal variability as a measure of comparison for experimental variations. Detailed comparisons of other investigations therefore appear unprofitable at this time.

The general plan of the investigation was to administer the different types of bismuth preparations, generally in the approximate clinical dosage, though with some of the compounds several doses were compared. The excretion was studied for single injections, weekly injections for three weeks, and "multiple" injections, viz., two or generally three a week for three weeks. The excreta were collected for a short period before the first injection to check whether the patient was already excreting bismuth, and the collection was continued for two or three weeks after the last injection. The total urine of each patient was analyzed daily; the feces were generally combined for the week. The fecal output, which averages perhaps a tenth of the urinary output, will be considered in a later paper. The studies on these patients were limited to their stay in the hospital. They are being supplemented by studies of later after-periods on patients who return to the hospital several weeks or months after routine treatment.

BISMUTH COMPOUNDS AND DOSAGE

Thus far these investigations have been chiefly concerned with the following preparations and doses (per injection):

(*A*) Water-Soluble Salts in Water:

Sodium bismuth tartrate, 42 mg. (32 mg. of bismuth) in 2 cc. Sodium bismuth citrate, 50 mg. (32 mg. of bismuth) in 2 cc. Also the same dosage of bismuth sodium citrate in ethylene glycol (2 cc.).

(*B*) Water-Soluble Salts Suspended in Oil:

Sodium potassium bismuth tartrate, 50, 75 and 100 mg. (32, 48 and 64 mg. of bismuth) in 1, 1.5 and 2. cc.

(*C*) Water-Insoluble Compounds Suspended in Oil:

Bismuth subsalicylate, 130 mg. (75 mg. of bismuth) in 1 cc.

(*D*) Oil Solutions of Liposoluble Compounds:

Quiniobine (quinine bismuth iodide dissolved in olive oil with lecithin), 60 mg. of bismuth (2 cc.). Bismo-cymol (bismuth camphocarboxylate), 75 and 100 mg. of bismuth (1.5 and 2 cc.). Biliposol (bismuth ethylmethyl nonoate), 80 mg. of bismuth (2 cc.).

ANALYTIC METHODS

The determination of bismuth was performed by a colorimetric method similar to that described by Leonard,[1] which was used by Mehrtens, Hanzlik and Marshall.[2] It depends on the formation of a double salt of bismuth and potassium iodide, having a yellow color. The oxidation is accomplished by nitric acid and hydrogen dioxide. Amounts ranging from 0.5 to 0.001 mg. of bismuth may be determined with an accuracy within from 0.001 to 0.005 mg. The method follows in detail.

Standards.—First, 0.2327 Gm. of bismuth nitrate is dissolved in dilute nitric acid and made up to 1 liter with water. One cubic centimeter of this solution contains 0.1 mg. of bismuth. Known amounts of the solution are added to 5 cc. of concentrated sulphuric acid and diluted with water to about 20 cc. After cooling, 4 cc. of 1 per cent sodium bisulphate is added, and the volume is made up to 25 cc. with water. Five cubic centimeters of 1.7 per cent potassium iodide solution is then added. The color thus given is matched in a colorimeter against an unknown quantity of bismuth prepared in the same manner.

Urine.—Samples of from 25 to 100 cc. of urine are digested by nitric acid in Kjeldahl flasks. The amount of nitric acid used is about 25 per cent of the volume of urine. When the solution is almost dry and light yellow, it is transferred to an evaporating dish and evaporated to dryness. The oxidation is completed from this point by heating over an open flame until the residue is white. Excessive heat must be avoided as bismuth is volatile at high temperatures. This residue is taken up with 5 cc. of sulphuric acid and 5 cc. of water and transferred to a Nessler tube graduated to 25 cc. The evaporating dish is rinsed with water and 4 cc. of 1 per cent sodium bisulphate, the washings are added, and the solution is made up to 25 cc. Five cubic centimeters of a 1.7 per cent solution of potassium iodide is added, a yellow color develops, and the solution is ready for comparison.

Feces.—Aliquot parts totaling approximately 300 Gm. of the weekly samples are used. The sample is digested in a 2 liter flask on a sand bath, nitric acid and hydrogen dioxide being added at intervals. Early in the digestion the fat separates and rises to the top of the solution. When this is cooled it may be removed and ignited with sodium nitrate, the residue being dissolved in water and added to the original. This considerably shortens the time required for oxidation. The heating of the solution is continued, with additions of nitric acid and hydrogen dioxide, the volume being reduced by evaporation, until the residue is entirely white after the nitric acid is evaporated. The residue is suspended in about 400 cc. of 5 per cent hydrochloric acid, and the bismuth is precipitated by hydrogen sulphide. The bismuth sulphide is collected on a filter and dissolved in nitric acid; the nitric acid is evaporated, and 5 cc. of sulphuric acid is added. The determination then proceeds as that on urine.

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RESULTS: URINARY EXCRETION OF BISMUTH FOR INDIVIDUAL PATIENTS

Charts 1 to 5 give a general picture of the phenomena, and as the graphs are drawn to scale they may also be used quantitatively. They are arranged according to the frequency of administration, generally in ascending order of excretion.

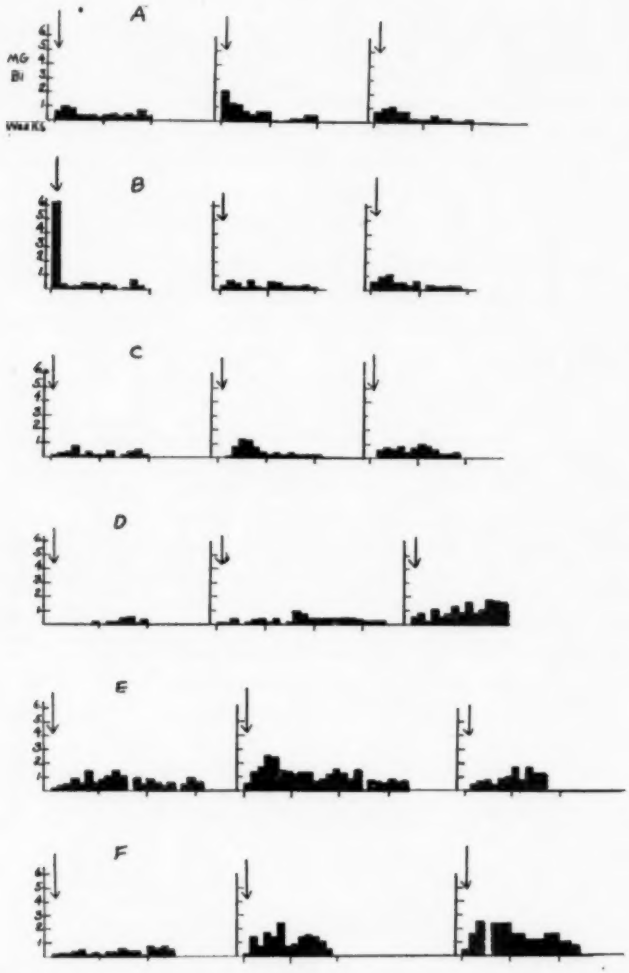

Chart 1.—Urinary excretion of bismuth after single injections: *A*, sodium bismuth citrate in water, 32 mg. of bismuth per dose; *B*, sodium bismuth citrate in ethylene glycol, 32 mg. of bismuth per dose; *C*, sodium bismuth tartrate in water, 32 mg. of bismuth per dose; *D*, potassium sodium bismuth tartrate in oil, 48 mg. of bismuth per dose; *E*, biliposol, 80 mg. of bismuth per dose; *F*, quiniobine, 60 mg. of bismuth per dose. The graphs show the daily urinary excretion of bismuth in milligrams. The arrow indicates the day of the injection. The lines beneath the graphs indicate weeks. The same arrangement is used in the succeeding charts.

Chart 1 shows the effects of single injections, beginning with the water-soluble compounds: *A*, sodium bismuth citrate in water; *B*, sodium bismuth citrate in ethylene glycol, and *C*, sodium bismuth tartrate in water. The dose corresponds to 32 mg. of bismuth. The excretion curves for all the patients are similar in magnitude and type, reaching a peak in from one to three days, with an asymptotic decline, at first steep, then slow. The first patient in *B* has an unusually high peak, doubtless owing to accidental injection into a vein. *D* shows the results of injection of an oil suspension of the water-soluble potassium sodium bismuth tartrate (48 mg. of bismuth). The excretion is similar in magnitude to that shown in *A*, *B* and *C*, but reaches its peak much more slowly, in one or two weeks. The curves, moreover, are more variable. These differences may be explained by the protective action of the oil film. *E* and *F* represent the effects of oily solutions, biliposol and quiniobine respectively. The type of the curve is altogether similar to that for the watery solutions, with a rapidly reached peak and a prompt initial decline. The excretion is somewhat higher, owing partly to the dose, corresponding to 80 and 60 mg. of bismuth respectively.

Chart 2 shows the effects of weekly injections of bismuth subsalicylate suspended in oil. The first three patients, *A*, *B* and *C*, received 75 mg. of bismuth for three injections, a total of 225 mg. of bismuth to approximate the dose of the other preparations. The excretion level is low and rises very slowly; indeed, the maximum is not reached until two or three weeks after the administration has been discontinued. The curve then falls slowly, becomes horizontal at about a third or half of its maximal level and remains so practically indefinitely, or at least for several months. This course differs materially from that with the other bismuth preparations, but is really an exaggeration of the features produced by the oil suspension of the tartrate. It shows very slow but continued absorption, which means a delay in the therapeutic effects but cumulation with successive doses, with eventual intensive effects tending to chronic poisoning. In harmony with this, it is noted that most of the clinical toxic symptoms, stomatitis, dermatoses and nephrosis, occurred with this preparation. Therefore, in eleven patients who had received the routine therapeutic course the later course of the excretion was again studied, larger doses being given for longer periods, generally 150 mg. of bismuth weekly to totals of from 540 to 4,125 mg. during from eight weeks to fourteen months. Samples of urine were collected generally for about a week, at different periods after the administration had stopped, up to six months. The results are shown in chart 2, *D* to *N*, arranged in ascending order of the total dosage of bismuth in the last course. A median curve drawn through these (chart 2, *O*) shows close agreement, the dotted lines representing the extremes and the heavy line the median for all the patients. With these higher and

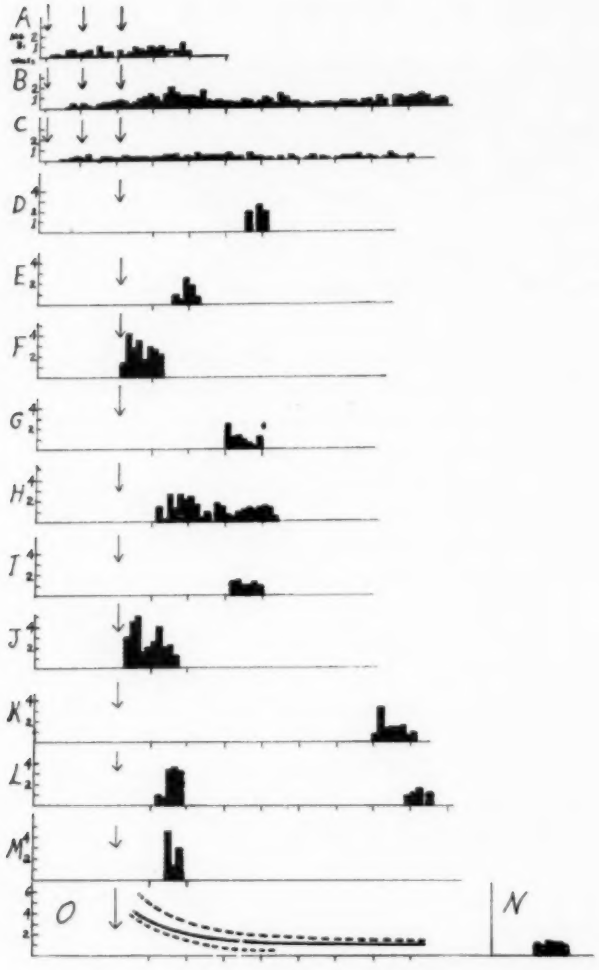

Chart 2.—Urinary excretion of bismuth after injections of suspensions of bismuth subsalicylate in oil. In patients *D* to *N*, the arrows represent the time of the last injection. Patients *A*, *B* and *C* each received 225 mg. of bismuth in three weeks. Patient *D* received 540 mg. mg. of bismuth in ten weeks; a dermatitis developed. Patient *E* received 1,650 mg. of bismuth in two and a half months and six months later 600 mg. of bismuth in four weeks, a total of 2,250 mg. Patient *F* received 1,275 mg. of bismuth in nine weeks. Patient *G* received 1,275 mg. of bismuth in eight weeks. Patient *H* received 1,500 mg. of bismuth in ten weeks. Patient *I*, who had stomatitis, received 1,425 mg. of bismuth in the form of salicylate and 152 mg. of bismuth as thio-bismol in three and a half months, a total of 1,577 mg. of bismuth. Patient *J* received 1,650 mg. of bismuth in two and a half months. Patient *K* received 1,725 mg. of bismuth in three months. Patient *L* received 1,750 mg. of bismuth and six weeks later 600 mg., a total of 2,325 mg. Patient *M* received 4,125 mg. of bismuth in fourteen months. Patient *N* received 1,850 mg. of bismuth; excretion studies were made six months later. In graph *O*, the central curve represents the smoothed median of all the patients. The dotted lines define the extremes.

more prolonged doses, the bismuth level at the end of the course is fairly high, but the total dosage within this range seems to have no effect on the excretion; presumably the remains of the earlier injections become walled off in time. The most striking feature again is the indefinitely long course of the excretion, which is still notable at the end of six months. It may be added that the excretion of the patients

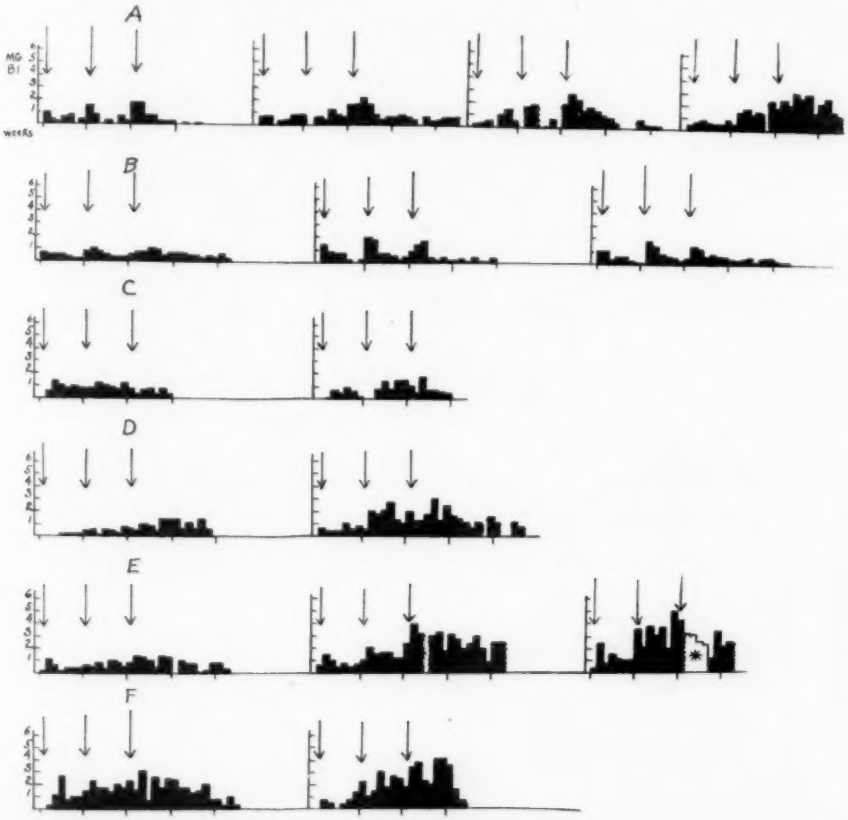

Chart 3.—Urinary excretion of bismuth after weekly injections of water-soluble compounds: *A*, sodium bismuth citrate in water, 32 mg. of bismuth per dose; *B*, sodium bismuth citrate in ethylene glycol, 32 mg. of bismuth per dose; *C*, sodium bismuth tartrate in water, 32 mg. of bismuth per dose; *D*, potassium sodium bismuth tartrate in oil, 32 mg. of bismuth per dose; *E*, potassium sodium bismuth tartrate in oil, 48 mg. of bismuth per dose; *F*, potassium sodium bismuth tartrate in oil, 64 mg. of bismuth per dose.

with toxic symptoms did not differ quantitatively from the excretion of those without toxic symptoms.

Chart 3 shows the effects of weekly injections of the water-soluble compounds: *A*, sodium bismuth citrate in water; *B*, sodium bismuth citrate in ethylene glycol, and *C*, sodium bismuth tartrate in water.

Each dose contained 32 mg. of bismuth, as in the experiments shown in chart 1. The curves are again essentially identical. They show a rapid ascent and a prompt sag after each injection. The second injection generally raises the peak considerably above that of the first; the third injection drives the peak still higher, except with the citrate in ethylene glycol, for which the third peak was slightly lower than the second. After treat-

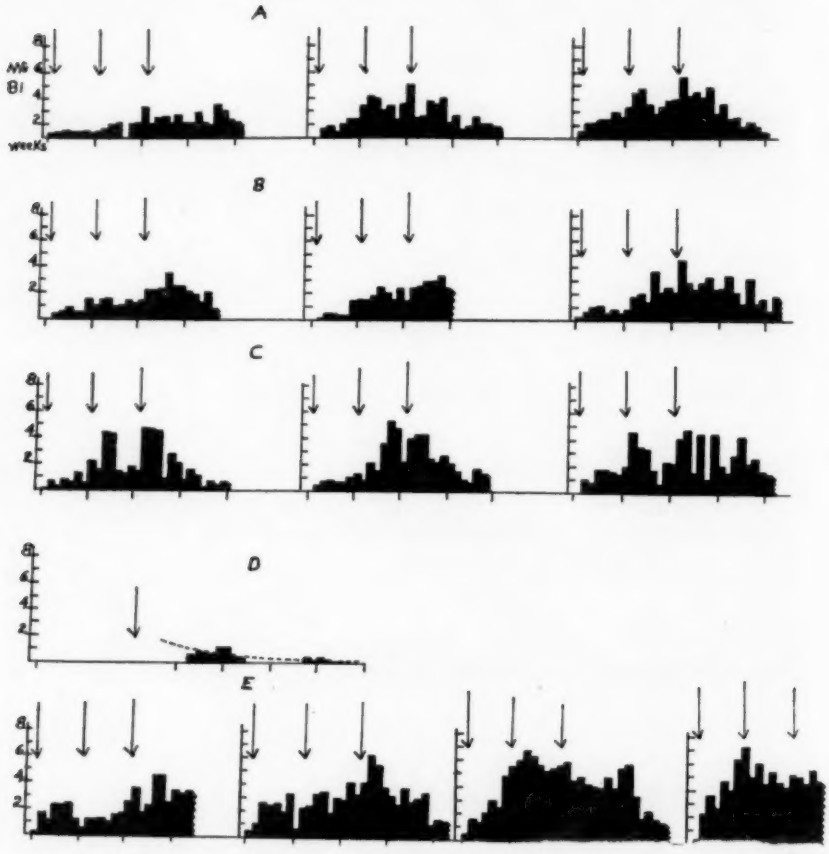

Chart 4.—Urinary excretion of bismuth after weekly injections of oil-soluble compounds: *A*, quiniobine, 60 mg. of bismuth per dose; *B*, bismo-cymol, 75 mg. of bismuth per dose; *C*, bismo-cymol, 100 mg. of bismuth per dose; *D*, bismo-cymol, after-period (the arrow indicates the last injection) with a total dose of 950 mg. of bismuth (toxicity); *E*, biliposol, 80 mg. of bismuth per dose.

ment is stopped the excretion falls rapidly in the form of a parabolic curve, just as with a single injection. Virtual zero would probably be reached in from thirty to thirty-five days. The tartrate in water produces a somewhat delayed peak, less sag between injections and a less rapid final descent, just as does a single injection of this solution.

again indicating a somewhat slower absorption. *D* shows the effects of the same dose (32 mg. of bismuth) of potassium sodium bismuth tartrate suspended in oil. The excretion is similar to that caused by the watery solutions, but the descent is more gradual, the absorption being prolonged by the protective action of the oil film. *E* and *F* represent the effects of larger doses of the tartrate. A dose of 48 mg. of bismuth (shown in *E*) gives considerably higher excretion, but 64 mg. (shown

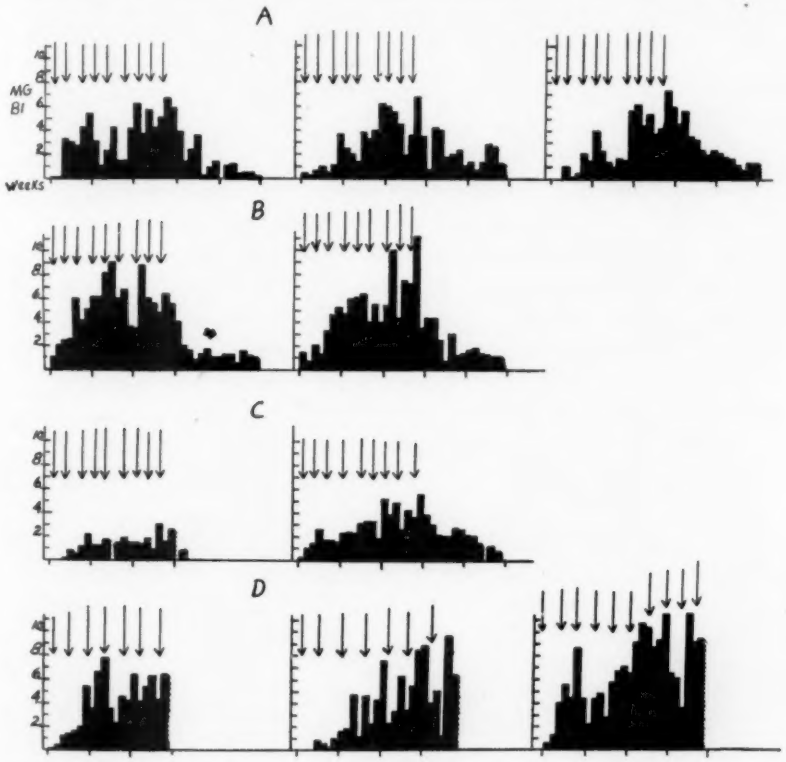

Chart 5.—Urinary excretion of bismuth after multiple injections: *A*, sodium bismuth citrate in water, 32 mg. of bismuth per dose; *B*, sodium bismuth citrate in ethylene glycol, 32 mg. of bismuth per dose; *C*, sodium bismuth tartrate in water, 32 mg. of bismuth per dose; *D*, biliposol, total dose 560 mg. of bismuth (the first patient), 320 mg. of bismuth (the second patient) and 800 mg. of bismuth (the third patient).

in *E*) does not raise this further. All the oil suspensions show the characteristic slowing of the descent.

Chart 4 illustrates the effects of weekly injections of oil solutions: *A*, quiniobine, in a dose of 60 mg. of bismuth; *B*, bismo-cymol, 75 mg. of bismuth; *C*, bismo-cymol, 100 mg. of bismuth, and *E*, biliposol, 80 mg. of bismuth. The excretion is materially higher than that for the

watery solutions, as shown in chart 3, owing partly to the higher dose. There is less sag between the injections; the peak generally rises parabolically to the last injection and then drops acutely as with the watery solutions. The curves differ from those for the oil suspensions in the more rapid rise and fall. The peak for the lowest oil solution, quiniobine (shown in *A*), is similar to that for the oil suspension of sodium bismuth tartrate in a dose of 48 mg. of bismuth (shown in chart 3, *E*). The curve for bismo-cymol, in a dose of 75 mg. of bismuth (shown in *B*), is similar in height and contour; and with a dose of 100 mg. of bismuth (shown in *C*) the excretion is but little more than that produced by the dose of 75 mg. of bismuth and much less than that produced by biliposol, in a dose of 80 mg. of bismuth (shown in *E*), which gives definitely the highest excretion. Bismo-cymol, therefore, is the least efficient. *D* shows the curve for a patient who received bismo-cymol equivalent to 950 mg. of bismuth in eleven weeks, the study being started ten days after the last injection because of toxic symptoms. It illustrates the asymptotic decline, projected as a dotted line, traces being excreted beyond a month.

Chart 5 illustrates the "multiple" injections, generally three a week for three weeks. With this frequency there is little sag between injections even with the watery solutions (*A, B* and *C*), and the rise proceeds parabolically to the last injection. The descent occurs promptly in the usual parabolic form. The excretion level is very much higher than with the weekly injections (chart 3, *A, B* and *C*) and is close to that produced by biliposol injected two or three times a week (*D*). The latter curve resembles that for the multiple injections of watery solutions closely in form as well as in height; it shows relatively little increase over that for single weekly injections (chart 4, *E*). The two curves for the citrate in ethylene glycol (*B*) are higher than those for the water citrate (*A*), but this difference is probably accidental, for it does not exist for the weekly or single injections.

CONCLUSIONS BASED ON STUDY OF EXCRETION OF BISMUTH FOR INDIVIDUAL PATIENTS

1. The resemblance between the different bismuth compounds is more striking than the differences, except for bismuth subsalicylate.

2. The rapidity of absorption, as reflected in the height, ascent and descent of the excretion curves, for these compounds is in the following descending order:

Watery solutions (sodium bismuth citrate in water or in ethylene glycol> sodium bismuth tartrate in water)>

Oil solutions (biliposol> quiniobine> bismo-cymol)>

Oil suspensions (potassium sodium bismuth tartrate> bismuth salicylate)

3. The peak of excretion increases in height with the number of injections, generally in a parabolic curve.

4. The peak increases with the dose, also parabolically; for instance, for sodium bismuth tartrate in oil the peak is twice as high with a dose of 48 mg. of bismuth as with 32 mg. of bismuth, but practically no more with 64 mg. of bismuth than with 48 mg. of bismuth. For bismo-cymol the peak is distinctly higher with 100 mg. than with 75 mg. of bismuth.

MEDIAN EXCRETION

To facilitate quantitative comparisons, the data for all patients with a given preparation, dosage and frequency of administration were reduced to medians which may be taken to represent type data. These

TABLE 1.—*Median Urinary Excretion of Bismuth (Milligrams per Week) During Last Week of Administration*

Preparation	Dose of Bismuth, Mg. per Injection	Weekly Excretion of Bismuth, Mg.		
		Single Injection 1st Week	Weekly Injection 3d Week	Multiple Injection 3d Week
Column: 1	2	3	4	5
Watery solutions	32	4.52	5.7	36.5
Sodium potassium bismuth tartrate in oil	32	2.54	9.88	
Sodium potassium bismuth tartrate in oil	48	4.3	19.1	
Sodium potassium bismuth tartrate in oil	64	5.56	18.47	
Bismuth salicylate	75	1.61	4.5	
Bismo-cymol	75	4.78	17.8	
Bismo-cymol	100	4.56	22.7	
Quiniobine	60	7.5	17.15	
Biliposol	80	11.83	25.92	37.3

are presented in line graphs. Chart 6 shows the total weekly excretion in successive weeks. The results for the watery solutions have been combined into a common median, since the variations between different preparations are less than those between different patients receiving the same preparation.

Single Injections.—These results are shown in the upper tier of chart 6, and numerically for the first week in column 3 of table 1. The highest weekly excretion median, that for biliposol (10.5 mg. of bismuth), is 7 times the lowest, that for the oil suspension of bismuth subsalicylate (1.6 mg. of bismuth). The next highest is that for another oil solution, quiniobine, (7.5 mg. of bismuth), and the next lowest is that for another oil suspension, sodium bismuth tartrate in a dose of 32 mg. of bismuth (2.5 mg. of bismuth). Doubling the dosage of the suspension of the tartrate doubles the excretion (5.6 mg. of bismuth). The excretion produced by the watery solutions (4.5 mg. of bismuth) is nearly 80 per cent higher that that produced by the oil-suspended tartrate. Bismo-cymol, in doses of 75 and 100 mg. of bismuth, causes an excretion of 4.8 and 4.6 mg. of bismuth, which is little

more than that for watery solutions in much smaller dosage. The results confirm that oil suspensions are absorbed less readily than watery solutions; that the relatively insoluble subsalicylate is absorbed more slowly; that the amount of oil-suspended tartrate absorbed increases with the dose; that the absorption of oil solutions differs for the individual drugs

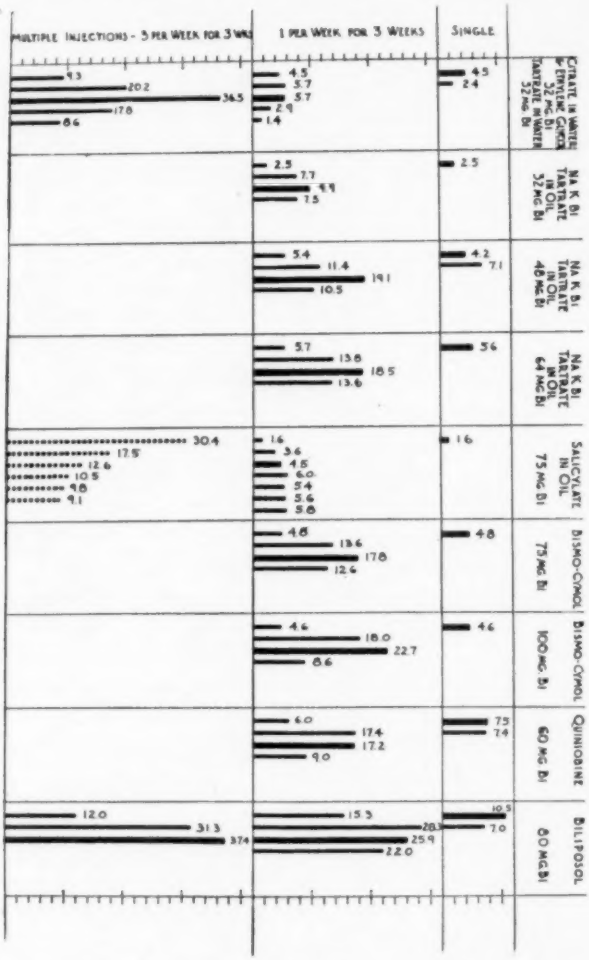
MULTIPLE INJECTIONS - 5 PER WEEK FOR 3 WKS
1 PER WEEK FOR 3 WEEKS
SINGLE
CITRATE IN WATER OF ETHYLENE CHLORIDE 32 MG. BI TARTRATE IN WATER 32 MG BI
NA K. BI TARTRATE IN OIL 32 MG BI
NA K. BI TARTRATE IN OIL 48 MG BI
NA K. BI TARTRATE IN OIL 64 MG BI
SALICYLATE IN OIL 75 MG BI
BISMO-CYMOL 75 MG BI
BISMO-CYMOL 100 MG BI
QUININOBINE 60 MG BI
BILIPOSOL 60 MG BI

Chart 6.—Median weekly urinary excretion of bismuth. This corresponds to the length of lines which are drawn to scale and also is shown as milligrams in the number above each line. The successive lines under each preparation represent successive weeks. The heavier line shows the last week of treatment, i. e., the week of the single injections and the third week of the weekly and multiple injections.

and is not proportional to their bismuth content, and that biliposol and quiniobine in the clinical dosage secure the largest amount of absorption.

If the second week is considered, it may be seen that the excretion has declined for the watery and oily solutions, but that with the oil-suspended tartrate the excretion is higher. This confirms the roentgen findings that the absorption of the suspension is incomplete in the first week and continues unabated in the second week.

Weekly Injections.—These results are shown in the second tier of chart 6. The heavier line in the third week marks the end of the injections and the beginning of the after-period. The excretion level increases parabolically with the successive injections. In the third or last week of

TABLE 2.—*Median Increment and Decrement Quotients of Weekly Urinary Excretion*

		Weekly Injections				Multiple Injections			
Column: 1	2	3	4	5	6	7	8	9	10
Preparation	Dose of Bismuth, Mg.	2d Week Divided by 1st Week	3d Week Divided by 2d Week	3d Week Divided by 1st Week	4th Week Divided by 3d Week	2d Week Divided by 1st Week	3d Week Divided by 2d Week	3d Week Divided by 1st Week	4th Week Divided by 3d Week
Watery solutions	32	1.3	1.0	1.2	0.51	2.1	1.8	2.8	0.48
Tartrate in oil	32	3.0	1.2	3.8	0.76				
Tartrate in oil	48	2.1	1.6	3.1	0.5				
Tartrate in oil	64	2.5	1.3	3.3	0.71				
Salicylate	75	2.2	1.3	2.7	1.3				
Bismo-cymol	75	2.9	1.3	3.7	0.71				
Bismo-cymol	100	3.9	1.2	4.9	0.38				
Quiniobine	60	2.9	0.98	2.8	0.53				
Biliposol	80	1.85	0.92	1.6	0.86	2.7	1.8	3.0	0.78

the administration it reaches the median amount shown in column 4 of table 1. These values represent considerable increases over the amounts for the first week, shown in column 3. The ascent of the excretion curves during the administration and their descent in the after-period may be expressed and compared quantitatively by the increment and decrement quotients, the total excretion for each week being divided by that for a preceding week, as in table 2. Column 5 in table 2 shows that the amount in the third week is from 1.2 times that of the first week for the watery solutions to 4.9 times that for bismo-cymol (dose, 100 mg. of bismuth). The quotient is above 3 for more than half of the preparations. The significance of this will be realized when it is remembered that 3 would be the maximal quotient if the first and second injections were still being absorbed at the same rate in the third week as in the first week, while it has been seen from single injections and will be seen again from the decrement quotients that the excretion declines rapidly in the week following the injection. Some other factor must be at work, presumably an increased excretion capacity of the kid-

neys, and perhaps partly a diuretic action of bismuth. Diuresis, however, is not the chief factor, for the increase of bismuth occurs when the volume of urine is not increased, and the rise in the excretion of bismuth is much greater than that in the volume of urine. That continued absorption of the earlier injections plays a definite, if subsidiary, part is indicated by the fact that all the oil suspensions (which are relatively slowly absorbed) show an excretion of from 2.7 to 3.8 times as much bismuth in the third week as in the first, while the most rapidly absorbed preparations show the lowest increment quotients, namely, 1.2 for watery solutions and 1.6 for biliposol. Chart 6 shows that the increase of excretion is almost always steeper in the second week than in the third, so that the curve is parabolic. This is probably due to some decline in the absorption from the first depot; beginning impairment of excretion capacity seems less probable. The decrease of excretion in the after-period was usually studied for only one week, the fourth. Column 6 in table 2 shows considerable differences in the decrement from the third to the fourth week. The salicylate gives a quotient (1.3) in harmony with its slow absorption. The decrease for the other preparations ranges from 0.86 mg. of bismuth (a drop of one-sixth) to 0.38 mg. of bismuth (a fall of nearly two-thirds). The median fall for all the preparations is about one-third, so that the rate of decline is fairly rapid. The sequence of the preparations in this respect appears irregular, presumably because it involves several factors which vary independently: the continuance of absorption, the level of excretion from which the fall starts, changes in excretion capacity, the mobilization of stored bismuth and probably other factors. In general, the curves for the suspensions fall more slowly than those for the solutions, the median quotient for the two groups being 0.73 and 0.51 respectively. This would be explained by the slower and more prolonged absorption of the suspensions.

The later course of the more prolonged therapeutic injections of the salicylate is shown in the broken line graph in the lower tier of chart 6. The median excretion attains the high level of 30 mg. of bismuth at the end of the injections, as much as that for any of the other preparations at the end of three weekly injections. The unique feature of the curve for the salicylate is the indefinite continuance of surprisingly high excretion levels long after the injections have been stopped; after six weeks and six months the median weekly urinary excretion is still from 9 to 10 mg. of bismuth, as high as in the third week of weekly injections of watery solutions or of tartrate suspensions in doses of 32 mg. of bismuth.

Multiple Injections.—The effects of multiple injections of watery solutions, three a week for three weeks, and of biliposol, two or three a week for three weeks, are shown in the lower tier of

chart 6. Suspensions were not included as they are not administered oftener than once a week in practice. The chart shows that the excretion level rises as usual with successive injections. The median excretion level for the watery solutions in the third and last week of the injections is 36.5 mg. of bismuth, over 6 times that for the weekly injections (table 1), although the amount injected was but 3 times as great. This is also reflected in the high increment quotients (table 2, columns 7 to 10). It is a further extension of the phenomenon noted in the comparison of the effects of weekly with those of single injections, which was attributed tentatively to increased renal permeability. The decrement quotient after the injections are discontinued is essentially the same as for the weekly injections, so that it is evidently not greatly influenced by the level of excretion. This is borne out by the data for other preparations. With multiple injections of biliposol the increase in excretion above that for the weekly injections is not nearly as marked as with the watery solutions; the median for the third week is but a half more than with the weekly injections, or 3 times that for the single injections. The total for the last week of the multiple injections of biliposol is practically the same as that for the multiple injections of watery solutions, although the difference is from 2½ to 4 times that for single and weekly injections. There seems to be a limiting factor at work, either in the absorption or in the excretion. The decrement quotient is practically the same as for the weekly injections.

PEAK OF EXCRETION: MAXIMAL INTENSITY OF THE URINARY OUTPUT OF BISMUTH

The peak of excretion reflects the maximal concentration in the blood, which is one of the important factors in the toxic and in the therapeutic action. To obviate accidental variations, the peak was taken as the mean of the three highest consecutive daily values. The median height for all the patients receiving each preparation is shown graphically and numerically in column 2 of chart 7. The number at the end of each line graph shows the peak of daily urinary excretion of bismuth in milligrams.

With single injections, illustrated in the first tier of chart 7, the peak increases from about 0.9 mg. of bismuth for the watery solutions to about 1.6 mg. for the tartrate in oil. It should be remembered that the dosage of bismuth also increases from 32 to 48 mg. The excretion with the oily solutions is intermediate, namely 1.3 mg. of bismuth for quiniobine and 1.5 mg. for biliposol, although the dosage of bismuth was higher (60 and 80 mg.).

With weekly injections the medians of the peaks of daily urinary excretion ranged between 1.2 and 5.7 mg. of bismuth, rising to from 1½ to 3½ times those for the single injections, similar to the increases in the weekly excretion. The lowest peak is that for the suspension of

the salicylate (1.2 mg. of bismuth); then come the watery solutions and the oil suspension of the tartrate with a dosage of 32 mg. of bismuth and excretion peaks of from 1.2 to 2.2 mg. of bismuth. Quiniobine is also within this range, with an excretion peak of 2.1 mg. of bismuth. Bismo-cymol, in a dosage of 75 mg. of bismuth, shows a

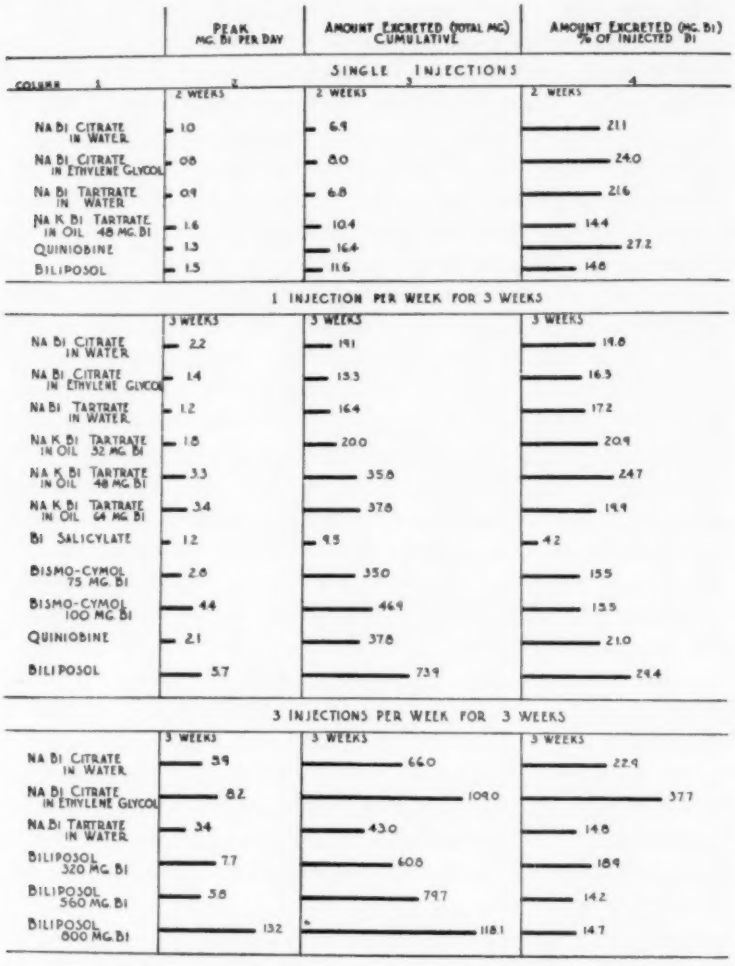
PEAK MG. BI PER DAY
AMOUNT EXCRETED (TOTAL MG.) CUMULATIVE
AMOUNT EXCRETED (MG. BI) % OF INJECTED BI
SINGLE INJECTIONS
COLUMN 1 2 3 4
2 WEEKS
NA BI CITRATE IN WATER 1.0 6.9 21.1
NA BI CITRATE IN ETHYLENE GLYCOL 0.8 8.0 24.0
NA BI TARTRATE IN WATER 0.9 6.8 21.6
NA K BI TARTRATE IN OIL 48 MG. BI 1.6 10.4 14.4
QUINIOBINE 1.3 16.4 27.2
BILIPOSOL 1.5 11.6 14.8
1 INJECTION PER WEEK FOR 3 WEEKS
3 WEEKS
NA BI CITRATE IN WATER 2.2 19.1 19.8
NA BI CITRATE IN ETHYLENE GLYCOL 1.4 13.3 16.3
NA BI TARTRATE IN WATER 1.2 16.4 17.2
NA K BI TARTRATE IN OIL 32 MG. BI 1.8 20.0 20.9
NA K BI TARTRATE IN OIL 48 MG. BI 3.3 35.8 24.7
NA K BI TARTRATE IN OIL 64 MG. BI 3.4 37.8 19.9
BI SALICYLATE 1.2 9.5 4.2
BISMO-CYMOL 75 MG. BI 2.8 35.0 15.5
BISMO-CYMOL 100 MG. BI 4.4 46.9 13.5
QUINIOBINE 2.1 37.8 21.0
BILIPOSOL 5.7 73.9 29.4
3 INJECTIONS PER WEEK FOR 3 WEEKS
3 WEEKS
NA BI CITRATE IN WATER 3.9 66.0 22.9
NA BI CITRATE IN ETHYLENE GLYCOL 8.2 109.0 37.7
NA BI TARTRATE IN WATER 3.4 43.0 14.8
BILIPOSOL 320 MG. BI 7.7 60.8 18.9
BILIPOSOL 560 MG. BI 5.8 79.7 14.2
BILIPOSOL 800 MG. BI 13.2 118.1 14.7

Chart 7.—Median peak of excretion. Cumulative excretion and percentile excretion. The lines are drawn to scale in each column (but the scale varies for the different columns). The amounts are expressed in numbers at the end of each line.

little higher peak, 2.8 mg. of bismuth; in a dosage of 100 mg., its peak is 4.4 mg. Doubling the dosage of the oil suspension of the tartrate also doubles its peak, 3.4 mg. of bismuth. The highest peak, 5.7 mg. of bismuth, is attained with biliposol.

Multiple injections raise the peak for the watery solutions to from 3.4 to 8.2 mg. of bismuth, about 3 to 5 times the peak for the weekly injections; the peaks for biliposol are raised to from 5.8 to 13.2 mg. of bismuth, not more than twice the weekly peaks, so that the increase is much less than for the watery solutions. The phenomenon was discussed in connection with the weekly excretion.

The dosage of bismuth is an important factor in determining the peak of excretion, as was stated in the grouping of the single and weekly injections. It was studied directly with three preparations. Weekly injections of sodium bismuth tartrate in oil, in doses of 32, 48 and 64 mg. of bismuth, gave median peaks of 1.8, 3.3 and 3.4 mg. of bismuth. Weekly injections of bismo-cymol, in doses of 75 and 100 mg. of bismuth, gave peaks of 2.8 and 4.4 mg. of bismuth. Multiple injections of biliposol, with totals of 320, 560 and 800 mg. of bismuth, gave peaks of 7.7, 5.8 and 13.2 mg. of bismuth. There is a definite tendency for the peak to increase with the dose. With the weekly injections of the tartrate in oil it reaches its limit at a dose of 48 mg. of bismuth, perhaps because the surface exposed to the solution does not increase as fast as the mass. With the weekly injections of bismo-cymol and the multiple injections of biliposol the peak rises until the administration of the highest dose, 100 mg. of bismuth per week for bismo-cymol and the total of 800 mg. of bismuth for biliposol.

Of the watery solutions, the citrate gives somewhat higher peaks than the tartrate in all three series, single, weekly and multiple injections, so that the difference is probably real although not important. With the citrate, the peak is higher for the watery solution than for the solution in ethylene glycol with single and weekly injections and lower with multiple injections; so the difference is probably accidental.

DURATION OF THE ASCENDING EXCRETION

The time required to reach the maximal excretion is shorter the more rapid the absorption, so it should be an index of the rate of absorption. Table 3 shows this as the interval between the first injection and the day when the highest urinary excretion was reached in the individual patients, making allowance for accidental variations. The simplest condition is that of single injections. Their medians are in the order of the watery solutions: citrate in water and in ethylene glycol, one day; tartrate in water, three days; biliposol, representing oil solutions, five days; tartrate in oil, representing oil suspensions, eleven days. This order agrees completely with the rapidity of absorption deduced from all lines of evidence. Quiniobine gave irregular data, from five to fifteen days. The weekly injections are complicated by the cumulative excretion, but the medians follow the same order: watery solutions, thirteen days; oil solutions, fifteen days; oil suspension of the tartrate, eighteen days, and oil suspension of the salicylate, twenty days.

With multiple injections the ascent continues somewhat longer, namely, for nineteen days with the watery solutions and for eighteen days with biliposol.

It may, therefore, be concluded that the duration is an index, inversely, of the rapidity of absorption, especially with single injections. With repeated injections it is complicated by the cumulative excretion but maintains the same sequence.

TABLE 3.—*Duration of Ascending Excretion* *

	Days to Peak	Median
Single Injections:		
Citrate in water	1, 1, 1	1
Citrate in ethylene glycol	1, 2	1
Tartrate in water	2, 3, 3	3
Tartrate in oil, 48 mg. of bismuth per dose	11, 11, 12	11
Biliposol	4, 5, 9	5
Quiniobine	5, 10, 15	10
Weekly Injections:		
Citrate in water	13, 15, 16, 16	15
Citrate in ethylene glycol	8, 8, 9	8
Tartrate in water	2, 17	
Median for all watery solutions	.....	13
Tartrate in oil, 32 mg. of bismuth	17, 18	
Tartrate in oil, 48 mg. of bismuth	12, 14, 19	
Tartrate in oil, 64 mg. of bismuth	18, 19	
Median for:		
All tartrate in oil	.....	18
Salicylate in oil	9, 20, 25	20
Bismo-cymol, 75 mg. of bismuth	16, 18, 21	18
Bismo-cymol, 100 mg. of bismuth	12, 15, 15	15
Quiniobine	14, 15, 24	15
Biliposol	7, 9, 17, 19	13
Median for all oil solutions	.....	15
Multiple Injections:		
Citrate in water	19, 19, 19	
Citrate in ethylene glycol	11, 18	
Tartrate in water	17, 20	
Median for all watery solutions	.....	19
Biliposol	9, 18, 19	18

* The interval between the first injection and the day when the highest level of urinary excretion was reached.

TOTAL OR CUMULATIVE URINARY EXCRETION

The excretion of small quantities of bismuth continues for periods much longer than it is feasible to keep patients under quantitative observation; nor would it have much practical value to do this, for it is safe to assume that these small amounts of bismuth do not produce therapeutic effects. It appeared preferable to confine the tabulation of the totals to the more active period of excretion, including the first two weeks for the single injections and three weeks for the weekly and multiple injections. The different methods of administration cover dif-

ferent after-periods and should therefore not be expressed in multiples of each other. However, the different preparations may be compared quantitatively for each of the methods. The median total, or, more properly, the cumulative excretion, is shown in chart 7 as milligrams in column 3 and as a percentage of the amount injected in column 4.

After single injections of all of the watery solutions, with a dosage of 32 mg. of bismuth, the cumulative excretion in two weeks amounts to from 6.8 to 8 mg. of bismuth; for the oil suspension of the tartrate, in a dose of 48 mg. of bismuth, it is 10.4 mg. of bismuth; for the solution of biliposol it is 11.6 mg. of bismuth, and for quiniobine it is 16.4 mg. of bismuth. The excretion of bismuth is, therefore, for the oil solutions about twice, and for the oil suspension, 1⅓ times, that for the watery solutions; however, there is also a difference in dosage, and when this is taken into account the order of the preparations is altered materially. According to the percentage of the injected doses excreted (column 4 of chart 7), the tartrate oil suspension ranks lowest, with 14.4 per cent, followed closely by biliposol, with 14.8 per cent. The excretion for the watery solutions, with percentages of from 21.1 to 24, is about 1½ times higher. Quiniobine ranks the highest, with 27.2 per cent.

With weekly injections, the cumulative excretion in three weeks is lowest for the salicylate, 9.5 mg. of bismuth, but it should be remembered that the excretion level of this compound continues to ascend beyond three weeks. Next come the watery solutions, with an excretion of from 15 to 19 mg. of bismuth. The oil suspension of the tartrate, in a dose of 32 mg. of bismuth, gives practically the same excretion, 20.9 mg., but with doses of 48 and 64 mg. the excretion is twice as high, 36 and 38 mg. Of the oil solutions the excretion for quiniobine, 38 mg., and that for bismo-cymol, 35 and 47 mg., are about 3 times as high as that for the watery solutions; and the excretion for biliposol, 74 mg., is 4 or 5 times that for the watery solutions. Expressed as the percentage of the amount injected, the salicylate gives by far the lowest excretion, 4.2 per cent. The watery solutions and the oil suspensions of the tartrate in doses of 32 and 64 mg. show practically the same values, from 17 to 21 per cent; the oil suspension of the tartrate in a dose of 48 mg. gives a somewhat higher excretion, 25 per cent. Of the oil solutions, the excretion for bismo-cymol (16 per cent) and that for quiniobine (21 per cent) are also practically the same as those for the watery solutions, but the excretion for biliposol (30 per cent) is nearly twice as high. Oil solutions as a class are, therefore, not absorbed better than watery solutions, but biliposol is superior in this respect.

With multiple injections, the excretion of the watery solutions is more variable, the medians ranging from 43 to 109 mg. This is from 2½ to 7 times the excretion with weekly injections, although the dose is but 3 times as great. The quantity equals or somewhat surpasses that for weekly injections of oil solutions. The cumulative excretion with multiple injections of biliposol is from 61 to 118 mg., which differs less from the excretion for watery solutions than does the excretion of biliposol with weekly injections. The percentile excretion with multiple injections of watery solutions, from 14.8 to 38, is generally higher than with the weekly injections, while that for biliposol, from 14 to 19, is but half of the weekly percentage. The explanation is obscure.

The effect of varying the dosage of a given preparation was studied for the following medians:

	Bismuth per dose (Mg.)	Amount Excreted (Mg.)	Per Cent Excreted
Tartrate in Oil	32	20.1	20.9
(Weekly)	48	35.8	24.7
	64	37.8	19.9
Bismo-Cymol	75	35.0	15.5
(Weekly)	100	47.0	15.5
	Total Dose	Amount Excreted	Per Cent Excreted
Biliposol	320	60.8	18.9
(Multiple)	560	79.7	14.2
	800	118.2	14.7

The changes of percentile excretion with the dosage are so inconstant and small that they are probably accidental, within the limits studied. Therefore, these variations of dosage do not materially affect the percentile excretion.

The two watery solutions gave the following median excretion, with equal doses.

	Per Cent of Excretion	
	Citrate	Tartrate
Single injections	21	22
Weekly injections	20	17
Multiple injections	23	15

The excretion for the tartrate is somewhat lower than that for the citrate, but the difference is not important.

The effects of the solvents, water and ethylene glycol, were compared for the citrate, as follows:

	Per Cent of Excretion	
	Citrate In Water	Citrate In Ethylene Glycol
Single injections	21	24
Weekly injections	20	16
Multiple injections	23	38

The difference is variable and therefore probably accidental.

The effects of watery solution and oil suspension were compared for weekly injections of the tartrate, in a dose of 32 mg. of bismuth. The difference in the excretion, 17 and 21 per cent, respectively, is not significant.

If one compares these observations on the cumulative excretion with those on the peak of excretion, the values will be seen to run fairly parallel and to lead to the same conclusions. Both are influenced chiefly by the dosage of bismuth, so that the percentile excretion of bismuth is confined within narrow limits for most preparations, namely, from one seventh to one fourth of the injected bismuth within two weeks after single injections, or within three weeks after from three to nine injections given in three weeks. The values for the salicylate are much lower, namely, one twenty-fifth, but this preparation is unique also in its long-continued excretion.

CLINICAL SIGNIFICANCE

The usefulness of a bismuth preparation involves the concentration of active bismuth attained in the tissues, especially in the blood, and the height, course, rise, duration and decline of this concentration. The present study clarifies these facts materially on the reasonable assumption that the urinary excretion of bismuth reflects the concentration of active bismuth in the blood. Clinical usefulness also involves other factors, such as pain of administration, convenience and cost, which are not involved in this inquiry.

The data confirm that the various bismuth preparations differ materially as to speed of absorption and furnish quantitative indexes of these differences. The preparations have a definite sequence in respect to rapidity of absorption: watery solutions> oil solutions> oil suspension of the tartrate> oil suspension of the salicylate. According to the duration of the excretion, and therefore of the concentration and action, the sequence runs in inverse order. The height of the concentration and the total amount of bismuth excreted, which together represent the intensity of the action, are fairly parallel and depend more on the dosage and the frequency of the injection than on any other factor; the salicylate, however, occupies a special position.

The various preparations have the following characteristics which would influence their clinical usefulness.

Watery Solutions of the Citrate and Tartrate and Solution of the Citrate in Ethylene Glycol.—The prompt absorption would make these preparations suitable for the rapid production of the effects of bismuth, although the oily solutions are practically as good in this respect. The more prompt absorption of the watery solutions, however, tends to remove them from the site of injection and thus to exhaust absorption depots; the concentration of bismuth is, therefore, not maintained with weekly administration, but rises and falls sharply with each injection. This periodicity can be obviated by giving injections three times a week. This secures smooth and high excretion curves, equal to those obtained with the oily solutions; but such multiple injections are inconvenient, especially since the injection of watery solutions is generally more or less painful. The chief value of the watery solutions would, therefore, be to speed the effects of bismuth. They are used before the more slowly absorbed oil suspensions of bismuth. The solution in ethylene glycol does not seem to offer any advantage over the watery solutions.

Oily Solutions.—These are essentially similar to the watery solutions in their absorption, but they differ practically because they are injected in higher doses, so that weekly injections suffice to produce relatively high and relatively lasting absorption, and the concentration curve is fairly smooth. It is, therefore, not necessary and indeed seems undesirable to inject them oftener than weekly. This is a material advantage, added to the fact that they often produce less local irritation than the watery solutions. However, the various oil solutions differ considerably. Biliposol is absorbed distinctly better than quiniobine, which offers little, if any, advantage over watery solutions. Bismo-cymol gives the poorest absorption of the oil solutions and is also the most irritant. Biliposol has what one would judge to be the most favorable absorption curve of any preparation tried and would seem to be a suitable form for routine use. However, it is doubtful whether in practice it is superior to the oil suspension of the tartrate in a dose of 48 mg. of bismuth.

Oil Suspension of Tartrate.—With this preparation, the concentration of bismuth rises promptly although more slowly than with either watery or oily solutions. Weekly injections give a satisfactory continuity of concentration. Multiple injections may be dangerous.

Oil Suspension of Bismuth Subsalicylate.—This preparation is an example of a water-insoluble basic bismuth salt. It differs markedly from the other preparations in that it is much more slowly absorbed and the effect is more lasting. There is a long delay before the effect of the bismuth is obtained, so that it is not advisable to start bismuth treat-

ment with this preparation unless its administration is begun well in advance, during arsphenamine therapy. The long-continued absorption is advantageous if the patient intermits treatment, but it may also lead to uncontrollable cumulation and consequent toxic effects. The small quantities of bismuth which are excreted over six months are perhaps more likely to injure the kidneys than is Spirochaeta pallida. All this throws doubt on the desirability of this preparation, at least for routine use. Briefly, then, the excretion curves indicate that the watery or oil solutions secure the most prompt effects, and that one oil solution and the oil suspension of the tartrate have advantages for routine use. The salicylate appears undesirable since its absorption is both too slow and too persistent.

SUMMARY

1. The urinary excretion of clinical doses of the following bismuth preparations was studied: watery solutions of sodium bismuth citrate and sodium bismuth tartrate, and a solution of the citrate in ethylene glycol; oily solutions (biliposol, quiniobine and bismo-cymol); oil suspensions (the water-soluble sodium potassium bismuth tartrate and the water-insoluble bismuth subsalicylate).

2. The resemblances in the excretion and therefore in the absorption and action of these preparations appear more impressive than the differences, except for the salicylate. This stands apart, with a much slower and much more persistent absorption and excretion.

3. Both the ascent and the descent of the excretion curve are parabolic, i. e., more rapid at first, then showing gradual and progressive slowing. The second injection raises the excretion often to more than double that for the first; succeeding injections give less rise, again in parabolic progression. The excretion sags more or less between weekly injections, in proportion to the rapidity of absorption. This is most marked with watery solutions, less marked with oil solutions, insignificant with the tartrate oil suspensions and absent with the salicylate. After discontinuing the injections, the abruptness of the descent depends chiefly on the continuance of absorption and is probably independent of the level of excretion of bismuth.

4. The velocity of excretion and absorption is in the following order: watery solutions > oil solutions > oil suspension of the tartrate > oil suspension of the salicylate. Among watery solutions the citrate is absorbed somewhat better than the tartrate. The citrate is absorbed equally well from the watery solution and from solution in ethylene glycol. For the oil solutions the absorption is in the following order biliposol > quiniobine > bismo-cymol.

5. The peak of excretion (the maximal concentration attained) and the total or cumulative excretion (within three weeks) run fairly parallel in the following general order: multiple watery solutions and multiple oil solutions> weekly oil solutions> weekly oil suspension of the tartrate> single oil solutions> weekly watery solutions> single oil suspension of the tartrate> single watery solutions> single oil suspension of the salicylate.

6. Except for the salicylate the peak and the total excretion are influenced more by the total dose of bismuth than by the nature of the bismuth compound.

7. The percentage excretion is, therefore, nearly uniform for all, from 15 to 25 per cent, within three weeks; it is much lower for the salicylate, 4 per cent, but here the excretion is very persistent, and a longer after-period would give relatively higher percentages.

8. The fecal excretion is being studied. It seems to be only about a tenth of the urinary excretion and fairly parallel to it.

TRANSITORY BALDNESS OF A PECULIAR TYPE FOLLOWING TRAUMA

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PROVIDENCE, R. I.

The following observation deals with a peculiar type of sudden and transitory baldness, presenting features both of alopecia areata and of alopecia diffusa, but distinctly different and, as far as I know, unique—a traumatic transitory alopecia of male pattern in a woman.

REPORT OF CASE

R. R., a white woman, 49 years old, single, of Irish descent, was born in Rhode Island. She has been an inmate of the State Hospital for Mental Diseases, Howard, R. I., since February, 1921, her condition having been diagnosed as epileptic psychosis with deterioration.

Her family history, in regard to abnormalities, premature loss of hair or signs of masculinity in women, reveals nothing significant.

On admission the hair was recorded as brown, with a few gray hairs. The distribution on the body was of the female type.

During her residence in the hospital the patient has been confused, assaultive, irritable and uncooperative. She has frequently injured herself by falls during epileptic seizures. During one seizure, on June 17, 1932, she fell and sustained a laceration 3 inches (7 cm.) long around the lambda. Because of her activity the wound could not be sutured cleanly. On October 26, it was reported that the wound was infected, with free edges. The pus was evacuated, and the wound was irrigated and painted with an antiseptic solution. No elevation of temperature was noticed. Occasionally the patient removed the dressing and put her fingers in the wound. In spite of this, on November 5 it was reported completely healed.

At about this time it was noted that hairs were falling rapidly from the top of the patient's head and from the temples. These regions were completely bald within a few days. I saw the patient on November 10. The top of her head was bald in the typical male pattern as shown in the figure (*A* and *B*). The rest of the hair was apparently normal macroscopically and on magnification. There was no loss of hair in patches on the rest of the scalp. A scar was visible near the lambda.

Examination of the rest of the body showed a moderate growth of coarse hair on the upper lip and the chin and a distribution of hair of female type on a normally feminine body. The uterus was infantile. No other abnormalities were detected.

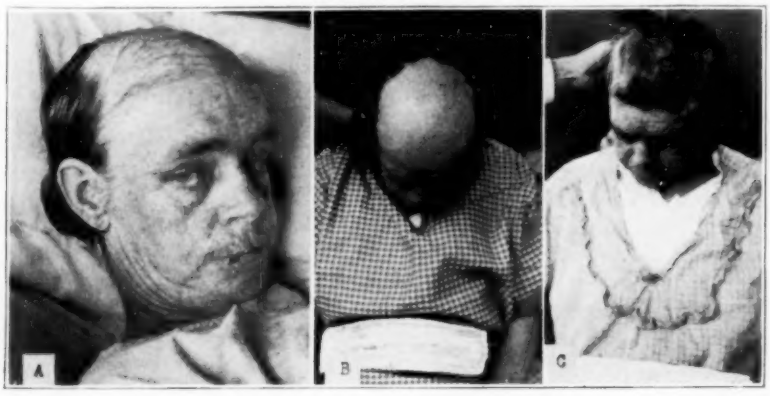
A basal metabolism test could not be made as the patient was uncooperative. The urine, blood count and blood chemistry were normal. The Wassermann and Kahn tests were negative. No bacteria were found on the roots of the hairs, and no growth of fungi was obtained in appropriate mediums. Roentgen examination of the skull did not show any pathologic changes. Epinephrine, pilocarpine, pituitary, thyroid and parathyroid extract were administered subcutaneously, but no apparent abnormalities in the function of the endocrinovegetative system were detected.

On Jan. 20, 1933, the bald area was completely covered with thin hairs about 1 cm. in length. On March 7, the length of the hairs was about 5 cm. (fig., *C*).

The patient was given ovarian extract by mouth and had the head rubbed with alcohol daily.

COMMENT

The views shown in the figure (*A* and *B*) are self-explanatory. The alopecia is distinctly of the premature seborrheic, hippocratic, or male type, so called because of the obscure, but established, fact, known from the time of Aristotle to that of Sabouraud, that children, eunuchs and women never become similarly bald. Seborrheic women may lose part of their hair permanently, but their baldness is never sharply limited to the top of the head and never leaves that area smooth, shiny and hairless as a billiard ball, as in man.



A and *B* show alopecia of male pattern in a woman following trauma to the head four months previously. *C* shows the recovering area about two months after the onset of the alopecia.

In the present case the pattern was extremely unusual, and the baldness was evidently not hippocratic, because of the history of a sudden development and a quick recovery. This was a case of alopecia following a trauma, which is rare in general and unique with this pattern, not having been recorded in either sex, so far as I know. The distribution of alopecia resulting from nervous shock is usually described as in patches or completely diffuse, but not limited to the top of the head.

The usual time from the shock to the falling of the hairs is from a few days to a few weeks. In the present case the time was about four months, although not only the wound itself but the subsequent complications must be taken into consideration as the acting cause.

Attention is called to the disproportion between the relatively slight trauma and the conspicuous loss of hair, and also to the psychic condition of the patient. Apparently there was a trophic nervous reaction of a distinctly reflex nature.

The patient has an infantile uterus and coarse hairs on the chin and lips. A dysfunction of the sexual glands may be considered as a tentative explanation of the unusual pattern.

Pituitary was not administered, and hence cannot be credited with the quick recovery, and psychotherapy could not be attempted.

SUMMARY

A peculiar case of traumatic transitory alopecia of male pattern in a woman is reported.

The cause of the peculiar pattern was probably a neuro-endocrine disturbance.

The mechanism appeared to be reflex, acting, probably, on the vasomotor nerves.

184 Waterman Street.

The results of laboratory examination and other data were obtained through the courtesy of Dr. Dimetra Tsina, assistant physician of the State Hospital for Mental Diseases, Howard, R. I.

VITILIGO FROM ARSPHENAMINE DERMATITIS AND FROM ARSENIC OF UNKNOWN ORIGIN

ARSENIC FINDINGS IN BLOOD, URINE AND SKIN

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AND
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Our interest in arsenic as a possible cause of vitiligo was aroused in October, 1930, when we first noticed the development of multiple snow-white spots on the skin of a Negro man, following the disappearance of a generalized arsphenamine dermatitis. Since that time we have seen two similar cases of vitiligo, both in Negroes, after arsphenamine dermatitis. In each case there was an increase of pigmentation in some areas, as well as apparent total absence in others, giving a very striking clinical picture. Because of this unusual finding, we undertook a study of the retention and elimination of arsenic, together with intradermal tests, to determine, if possible, the rôle played by arsenic in the development of these clinical symptoms.

On analyzing our clinic reports of the cases, we found certain factors common to all three:

1. The three patients were full-blooded Negroes.

2. Each had areas of total absence of pigment and areas with increased pigment.

3. The pigmentary changes followed arsenical dermatitis, except that one patient had two very small vitiligo spots before the dermatitis.

4. All showed retention of arsenic, which was found in abnormal amounts in the blood, urine and skin. Sections of skin, both from pigmented and nonpigmented areas, revealed granules of arsenic.

5. All gave positive reactions to skin tests with different arsphenamines injected intradermally in minute quantities.

Our study of the three cases of vitiligo following arsphenamine dermatitis, with our findings of evidence of arsenic retention, caused us to wonder if arsenic might not be one of the causes of vitiligo occurring in patients who had no history of arsenic intake, and led us to

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From Vanderbilt Clinic, Columbia University, College of Physicians and Surgeons.

investigate a series of seven of these patients for evidences of retention of arsenic. Our findings may be summarized as follows:

1. Six persons showed abnormal amounts of arsenic in the blood, urine or skin. Some of these patients revealed very high amounts of arsenic in the skin, both by chemical and by histologic examinations —one as high as 5.22 mg. per hundred grams of dried specimen, the greatest quantity of arsenic we ever found in a section of human skin. In six of the seven cases, sections of skin prepared for microscopic examination for arsenic showed the presence of granules of arsenic trisulphide in greater or lesser quantities.

2. Of the four patients in this group tested with intradermal injections of arsphenamine, all gave positive reactions.

All cases of vitiligo taken collectively, three occurring after arsphenamine dermatitis and seven without a history of arsenic intake, show a striking similarity in the retention of arsenic, even greater quantities being found in patients not treated with arsphenamine. All of these patients who were tested intracutaneously with arsphenamine gave positive reactions.

RESULTS OF INVESTIGATION

The following pages present in more detailed form the results of our investigation of the ten cases.

HISTORY AND CRITIQUE

Considering the great variety of sources—medicinal, industrial, criminal and accidental—from which arsenic may find its way in toxic quantities into the human system, it might at first appear strange that the general literature on arsenic poisoning should afford but scant mention of pigmentary disturbances. Toxicologists, of course, are concerned primarily with the more serious symptoms and evidences of acute poisoning, especially in internal organs. Dermatologists have devoted their attention to the more striking eruptive manifestations of arsenism. In many monographs on arsenic in the treatment of chorea and other conditions, pigmentary disturbances are barely mentioned, if at all, among the possible complications. The special literature is a literature of melanoderma. Even Imbert-Gourbeyre, in his detailed study of the effects of arsenic on the skin, did not report a single case of depigmentation, unless we include blanching of the hair and eyebrows, in the case of the chemist, Schindler, from inhalation of arseniuretted hydrogen; and the sudden blanching of hair is generally conceded to have an entirely different mechanism from that of the loss of skin pigment. Brooke and Roberts, describing the extensive series of cases of arsenical beer poisoning, evidently did not observe any vitiligo among the

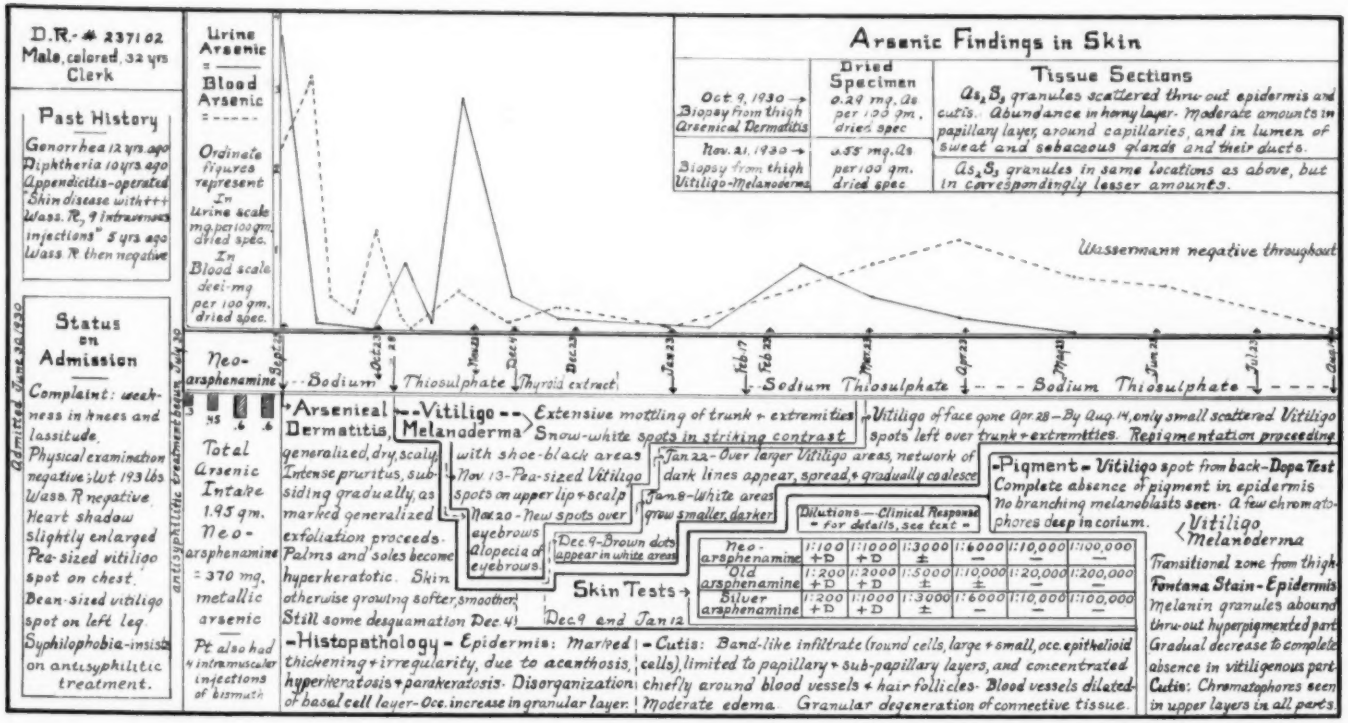
D.R.- # 237102
Male, colored, 32 yrs
Clerk
Past History
Gonorrhea 12 yrs. ago
Diphtheria 10 yrs. ago
Appendicitis-operated
"Skin disease with +++
Wass. R, 9 intravenous
injections" 5 yrs. ago
Wass. R then negative
Status on Admission
Complaint: weakness in knees and lassitude.
Physical examination negative; Wt 193 lbs
Wass. R negative.
Heart shadow slightly enlarged
Pea-sized vitiligo spot on chest.
Bean-sized vitiligo spot on left leg
Syphilophobia-insists on antisyphilitic treatment.
Admitted June 30, 1930
antisyphilitic treatment June 30
Urine Arsenic
Blood Arsenic
Ordinate figures represent
In Urine scale mg. per 100 gm. dried spec.
In Blood scale decimg per 100 gm. dried spec.
Arsenic Findings in Skin
Dried Specimen
Tissue Sections
Oct 9, 1930 → Biopsy from thigh Arsenical Dermatitis
0.29 mg. As per 100 gm. dried spec
As2S3 granules scattered thru-out epidermis and cutis. Abundance in horny layer. Moderate amounts in papillary layer, around capillaries, and in lumen of sweat and sebaceous glands and their ducts.
Nov. 21, 1930 → Biopsy from thigh Vitiligo-Melanoderma
0.55 mg. As per 100 gm. dried spec
As2S3 granules in same locations as above, but in correspondingly lesser amounts.
Wassermann negative throughout
Sept 25
Oct 13
28
Nov 13
Dec 4
Dec 23
Jan 23
Feb 17
Feb 28
Mar 23
Apr 23
May 21
Jun 23
Jul 23
Aug 4
Neo-arsphenamine
Sodium Thiosulphate
Thyroid extract
Sodium Thiosulphate
Sodium Thiosulphate
.5
.45
.6
.6
Total Arsenic Intake 1.95 gm.
Neo-arsphenamine = 370 mg. metallic arsenic
Pt also had 4 intramuscular injections of bismuth
Arsenical Dermatitis
generalized, dry, scaly
Intense pruritus, subsiding gradually, as marked generalized exfoliation proceeds.
Palms and soles become hyperkeratotic. Skin otherwise growing softer, smoother
Still some desquamation Dec 4
Vitiligo -- Melanoderma
with shoe-black areas
Nov 13-Pea-sized Vitiligo spots on upper lip + scalp
Nov 20-New spots over eyebrows
Alopecia of eyebrows
Extensive mottling of trunk + extremities
Snow-white spots in striking contrast
Jan 22-Over larger Vitiligo areas, network of dark lines appear, spread + gradually coalesce
Jan 8-White areas grow smaller, darker
Dec 9-Brown dots appear in white areas
Skin Tests →
Dec 9 and Jan 12
Dilutions — Clinical Response — for details, see text —
Neo-arsphenamine 1:100 +D 1:1000 +D 1:3000 ± 1:6000 — 1:10,000 — 1:100,000 —
Old arsphenamine 1:200 +D 1:2000 +D 1:5000 ± 1:10,000 ± 1:20,000 — 1:200,000 —
Silver arsphenamine 1:200 +D 1:1000 +D 1:3000 ± 1:6000 — 1:10,000 — 1:100,000 —
Vitiligo of face gone Apr 28 — By Aug 14, only small scattered Vitiligo spots left over trunk + extremities. Repigmentation proceeding
-Pigment - Vitiligo spot from back - Dopa Test
Complete absence of pigment in epidermis
No branching melanoblasts seen. A few chromatophores deep in corium.
Vitiligo Melanoderma
Transitional zone from thigh
Fontana Stain - Epidermis
Melanin granules abound thru-out hyperpigmented part
Gradual decrease to complete absence in vitiligenous part
Cutis: Chromatophores seen in upper layers in all parts.
-Histopathology - Epidermis: Marked thickening + irregularity, due to acanthosis, hyperkeratosis + parakeratosis. Disorganization of basal cell layer-Occ. increase in granular layer.
- Cutis: Band-like infiltrate (round cells, large + small, occ. epithelioid cells), limited to papillary + sub-papillary layers, and concentrated chiefly around blood vessels + hair follicles. Blood vessels dilated. Moderate edema. Granular degeneration of connective tissue.

Fig. 1.—Report of case 1 and chart showing arsenic in the blood, urine and skin. In this and the following illustrations dopa is the initial abbreviation for dioxyphenylalanin.

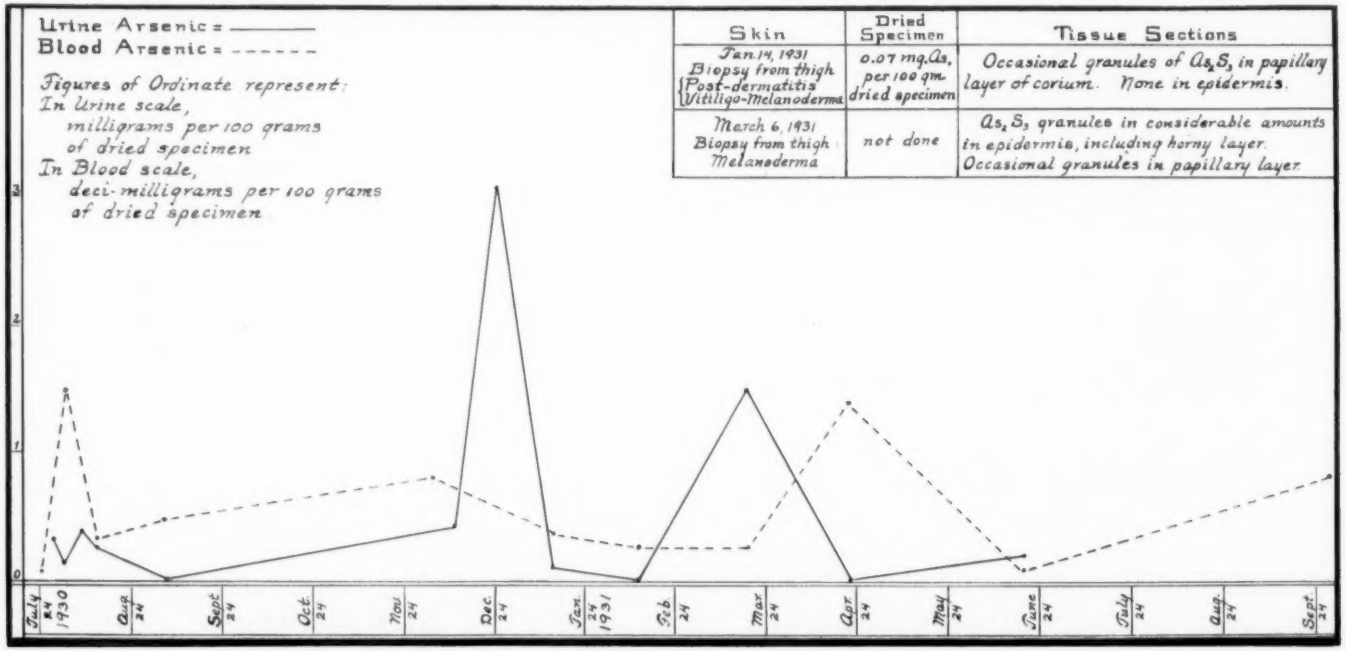

Fig. 2a (case 2).—Chart showing arsenic in the blood, urine and skin.

I.T. # 244828
Female, colored, 39 yrs.
Housewife
Admitted Feb 2, 1930 for positive Wassermann.
Weight: 122 pounds.
Blood pressure: 132/85
Deep reflexes of upper and lower extremities equal and hyperactive.
Right pupil slightly irregular; slight nystagmus to right. Pubic hair deficient in some.
Thyroid enlargement.
Previous History
Malaria at 15 years.
Left facial neuralgia for about 20 years.
Bilateral ovariectomy + appendectomy 10 yrs. ago. Since then, hot flashes, obstinate constipation; easily fatigued.
Married 10 years.
No pregnancies.
Syphilis I and II denied both by name and symptom.
Cathartics and patent nerve tonics during past 4 years.
Neo-arsphenamine
Feb. 28 – May 1
.15 .25 .3 .45 .45
.5 .55 .55 .6
Total Arsenic Intake 3.8 gm.
Neo-arsphenamine = 722 mg. metallic arsenic
Pt. also had 9 intramuscular injections of bismuth
After 12 wks' lapse she returned to Clinic with arsenical dermatitis July 24, 1930
1930 1931
Blood – Wassermann – negative
Sodium Thiosulphate – 15 grams in 16 injections
Bismo-Cymol – 1.8 grams in 12 injections
Mercury Salicylate 1/10 grain in 10 injections
Spinal Fluid negative
Arsenical Dermatitis – Melanoderma
Maculo-papular rash, dating from June, over neck, chest, back + arms. July 24: Brownish-black spots visible on sites of rash, also on mucous membrane of mouth. Generalized seborrheic exfoliation. July 31: Spots darker, and covered with easily detached scales. Aug. 14: Spots still darker – shoe-black mottling. Skin dry; intense pruritus. By end of September, dermatitis cleared up, but black spots remain, and new ones appear.
Histopathology – Post-dermatitis Melanoderma
Changes limited to epidermis + upper portion of cutis.
Epidermis: Irregular thickening, due to edema, disorganization of basal cell layer, increase in granular layer, moderate hyperkeratosis + parakeratosis.
Cutis: Moderate round cell infiltration around blood vessels; moderate edema; dilatation of blood vessels and perivascular lymph spaces.
Pigment: Yellow-brown pigment, pronounced in basal cell layer and immediately beneath, where it is clumped around blood vessels and hair follicles; also in lymph spaces. Pigment both intracellular and extracellular.
Vitiligo – Melanoderma – Dec. 31 – Jan. 7: Two snow-white, dime-sized Vitiligo spots noticed on chest, one on chin; areas of hypopigmentation on upper lip. New hyperpigmented spots appear on face and spread over cheeks. Jan. 7: During next few weeks, pin-head sized Vitiligo spots dotted over hands, thighs, scalp. Feb. 4: Black spots on face, trunk, and extremities begin to fade, first in center, then toward periphery. March-June: Repigmentation of vitiligenous areas beginning: pigmented islands form in centers, while pigment also spreads inward from borders. By July, Vitiligo areas greatly diminished in size, and irregular in outline. Repigmentation continuing. By September 1931, dark spots still noticeable, but fading slowly.
Pigment Findings in Biopsies Taken from Areas of Vitiligo Melanoderma
(1) Vitiligo spot from chest (Fontana Stain): Epidermis practically devoid of pigment, but pigment still present in chromatophores of corium.
(2) Normal and hyperpigmented areas from thigh – transitional zone (Fontana Stain): Abundance of melanin in hyperpigmented part, especially in basal cell layer. Many chromatophores present in corium.
(3) Vitiligo spot from neck in process of repigmentation (Dopa Test): Plenty of pigment in epidermis; dendritic melanoblasts seen in basal layer. Many chromatophores present in corium.
Skin Tests – Dilutions and Clinical Response
December 31 | March 18 | May 6
Neo-arsphenamine: 1:100 – | 1:10,000 – | 1:100,000 – | 1:100 +D | 1:100 ±
Old arsphenamine: 1:200 – | 1:20,000 – | 1:200,000 – | 1:200 + | 1:200 ±
Silver arsphenamine: 1:200 – | 1:10,000 – | 1:100,000 – | 1:200 +D | 1:200 ±
[+] On site of injection, nodule appears within a few days to 2-3 weeks, + remains from a few weeks to several months.
[+D] As above, but accompanied by scaling dermatitis around injection site.
[±] Papule or nodule, with or without scaling; disappears within 1-2 weeks.
[–] Negative; or transitory macule, which disappears within first few days.

Fig. 2b.—Report of case 2.

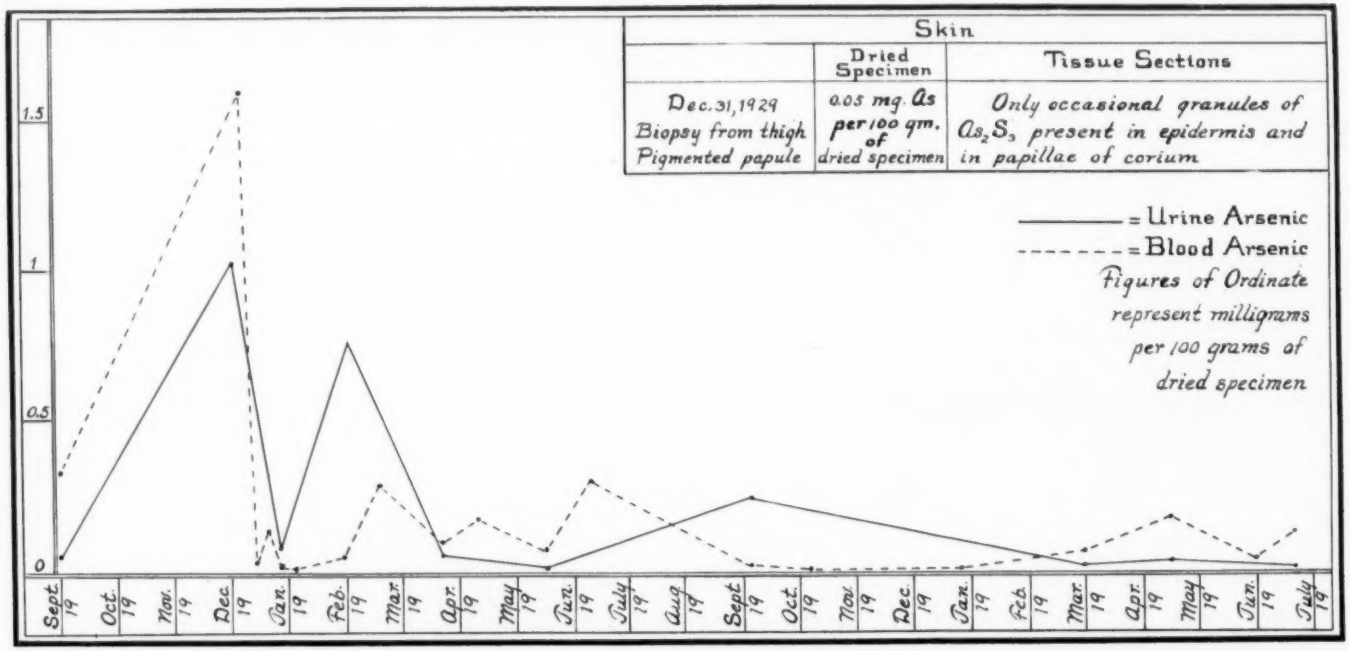

Fig. 3a. (case 3).—Chart showing arsenic in the blood, urine and skin.

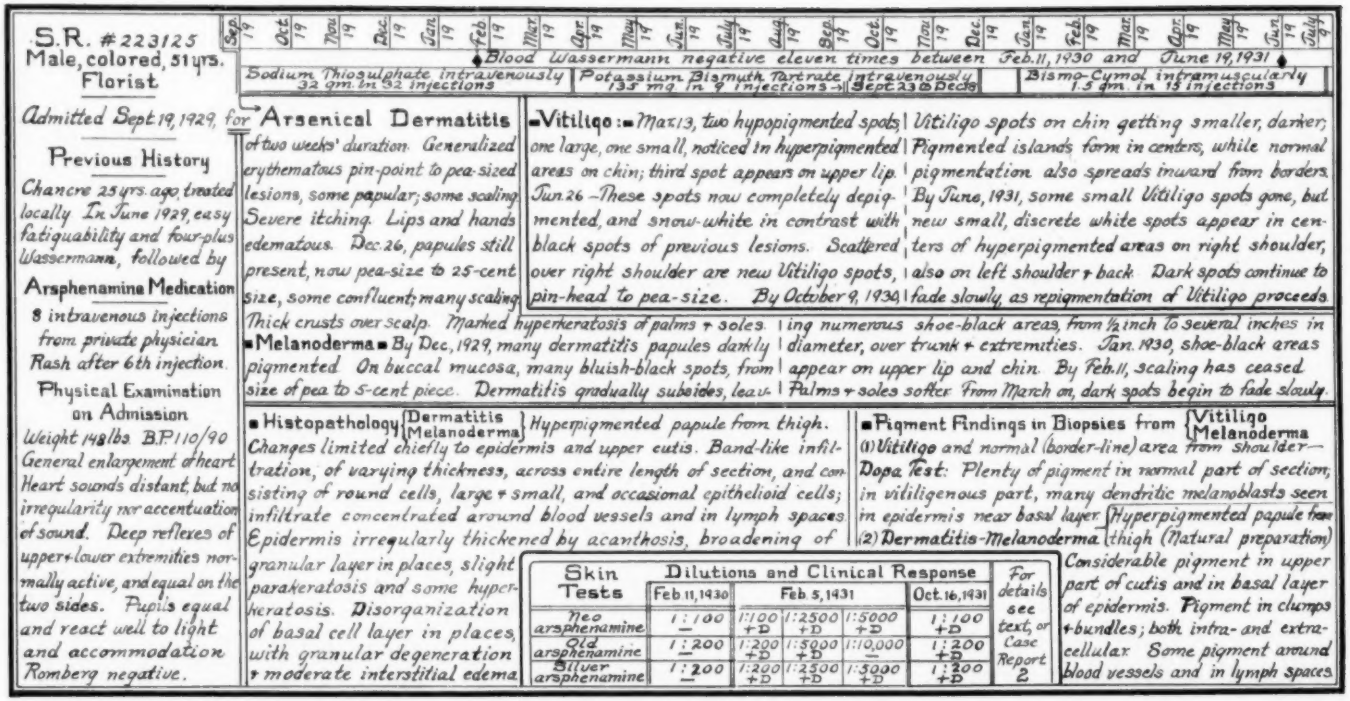
S.R. #223125
Male, colored, 51 yrs.
Florist
Admitted Sept. 19, 1929, for Arsenical Dermatitis
Previous History
Chancre 25 yrs. ago, treated locally. In June 1929, easy fatiquability and four-plus Wassermann, followed by
Arsphenamine Medication
8 intravenous injections from private physician. Rash after 6th injection.
Physical Examination on Admission
Weight 148 lbs. B.P. 110/90. General enlargement of heart. Heart sounds distant, but no irregularity nor accentuation of sound. Deep reflexes of upper + lower extremities normally active, and equal on the two sides. Pupils equal and react well to light and accommodation. Romberg negative.
Sep 19 Oct 19 Nov 19 Dec 19 Jan 19 Feb 19 Mar 19 Apr 19 May 19 Jun 19 July 19 Aug 19 Sep 19 Oct 19 Nov 19 Dec 19 Jan 19 Feb 19 Mar 19 Apr 19 May 19 Jun 19 July 19
Blood Wassermann negative eleven times between Feb. 11, 1930 and June 19, 1931
Sodium Thiosulphate intravenously 32 gm. in 32 injections
Potassium Bismuth Tartrate intravenously 1.35 mg. in 9 injections
Sept. 23 to Dec. 9
Bismo-Cymol intramuscularly 1.5 gm. in 15 injections
Arsenical Dermatitis of two weeks' duration. Generalized erythematous pin-point to pea-sized lesions, some papular; some scaling. Severe itching. Lips and hands edematous. Dec. 26, papules still present, now pea-size to 25-cent size, some confluent; many scaling. Thick crusts over scalp. Marked hyperkeratosis of palms + soles.
Melanoderma. By Dec., 1929, many dermatitis papules darkly pigmented. On buccal mucosa, many bluish-black spots, from size of pea to 5-cent piece. Dermatitis gradually subsides, leaving numerous shoe-black areas, from ½ inch to several inches in diameter, over trunk + extremities. Jan. 1930, shoe-black areas appear on upper lip and chin. By Feb. 11, scaling has ceased. Palms + soles softer. From March on, dark spots begin to fade slowly.
Vitiligo: Mar. 13, two hypopigmented spots, one large, one small, noticed in hyperpigmented areas on chin; third spot appears on upper lip. Jun. 26 – These spots now completely depigmented, and snow-white in contrast with black spots of previous lesions. Scattered over right shoulder are new Vitiligo spots, pin-head to pea-size. By October 9, 1930, Vitiligo spots on chin getting smaller, darker; Pigmented islands form in centers, while normal pigmentation also spreads inward from borders. By June, 1931, some small Vitiligo spots gone, but new small, discrete white spots appear in centers of hyperpigmented areas on right shoulder, also on left shoulder + back. Dark spots continue to fade slowly, as repigmentation of Vitiligo proceeds.
Histopathology {Dermatitis / Melanoderma} Hyperpigmented papule from thigh. Changes limited chiefly to epidermis and upper cutis. Band-like infiltration, of varying thickness, across entire length of section, and consisting of round cells, large + small, and occasional epithelioid cells; infiltrate concentrated around blood vessels and in lymph spaces. Epidermis irregularly thickened by acanthosis, broadening of granular layer in places, slight parakeratosis and some hyperkeratosis. Disorganization of basal cell layer in places, with granular degeneration + moderate interstitial edema.
Pigment Findings in Biopsies from {Vitiligo / Melanoderma}
(1) Vitiligo and normal (border-line) area from shoulder—
Dopa Test: Plenty of pigment in normal part of section; in vitiligenous part, many dendritic melanoblasts seen in epidermis near basal layer.
(2) Dermatitis-Melanoderma {Hyperpigmented papule from thigh (Natural preparation)} Considerable pigment in upper part of cutis and in basal layer of epidermis. Pigment in clumps + bundles; both intra- and extracellular. Some pigment around blood vessels and in lymph spaces.
Skin Tests
Dilutions and Clinical Response
Feb 11, 1930
Feb 5, 1931
Oct. 16, 1931
For details see text, or Case Report 2
Neo arsphenamine: 1:100 — | 1:100 +D | 1:2500 +D | 1:5000 +D | 1:100 +D
Old arsphenamine: 1:200 — | 1:200 +D | 1:5000 +D | 1:10,000 — | 1:200 +D
Silver arsphenamine: 1:200 — | 1:200 +D | 1:2500 +D | 1:5000 +D | 1:200 +D

Fig. 3b.—Report of case 3.

melanoses, although spotted forms were common. Depigmentation, however, might have been present, though masked by other cutaneous manifestations, and hence ignored in the reporting; for example, Van Kerckhoff recently established that there was complete absence of pigment in the psoriatic papule and the psoriasiform syphilitic papule, a condition hitherto unsuspected because of the ruddy hue imparted by the inflammatory changes.

The first case in which we find mention of a loss of pigment definitely attributed to arsenic is that reported by Dreysel in 1897. This was a case of white and brown mottling on a man previously treated with a solution of potassium arsenite for lichen ruber planus. Dreysel described the spots (both brown and white) as being sharply defined, pinhead to lentil-sized, and most numerous on the face and thorax; some were isolated, others in small groups. The remaining lichen nodules, not especially numerous, were scattered chiefly over the sacral region and the buttocks. The general color of the skin was a light brown. This patient also had hyperkeratosis of the palms and soles and symptoms of peripheral neuritis, which had grown worse under continued arsenical medication, although the lichen nodules practically disappeared. Microscopically, the white spots proved to be entirely devoid of pigment in the horny layer; the rete showed only traces of pigment, and that in the lowermost layers; there was plenty of pigment in the cutis, and no considerable infiltration. Dreysel considered the hyperpigmented spots to be outgrowths of receded lichen nodules, but attributed the depigmented spots to arsenic, maintaining that the atrophic and sclerotic forms of depigmentation following lichen plaques —as described by Darier and others—are really scar formations, and that such changes are entirely absent in the present instance. Dreysel believed this to be the first report of depigmentation of this kind.

In the quite extensive literature on arsenical melanosis of the pre-arsphenamine era, although spotted forms are common, one finds only an occasional mention of depigmentation, the interest obviously being centered on the hyperpigmentation. Roscher, in 1907, demonstrated before the Berlin Dermatological Society a patient who had previously been treated with arsenic (preparation and amount not given) for an itchy eruption suggestive of mycosis fungoides. A generalized melanoderma developed in which appeared round depigmented spots, lentil to coin-sized, scattered over the entire body. Although Roscher's diagnosis of "arsenical melanosis" does not seem to have been questioned at the time, the white spots—as in the Dreysel case—were suspected by other observers of being merely the residue of the original dermatosis, and not related to the arsenic.

Seven years before this, Rosenthal had described, under the title "leukoderma post-psoriaticum," a case of extensive leukoderma, con-

TABLE 1.—*Case Reports 4 to 10; Vitiligo With Evidence of Arsenic in System But Without History of Arsenic Intake*

Patients	Pigment: Clinical	Pigment: Histologic	Arsenic: Blood and Urine (In Mm. per 100 Gm. of Dried Specimen)		Arsenic: Skin (Dried Specimen and Tissue Sections)	Intradermal Tests with Arsphenamines
			Blood	Urine		
4. T. L., male, white, 21 years of age, bank clerk, under observation since Aug. 26, 1930	Vitiligo first noticed 4 yrs. ago; on admission, numerous large, irregular, sharply defined patches, completely depigmented, over face, body and extremities; several of the vitiligo spots developed around pigmented hairy moles on neck and back; areas of gray hair on scalp and pubis	Biopsy from back; borderline of normal skin and vitiligo. Fontana stain: normal distribution of pigment in first section; absence of pigment in second (vitiliginous) section Pathology: no pathologic changes other than loss of pigment	Feb. 2, 1931 April 21, 1931 May 12, 1931 May 14, 1931 May 26, 1931 June 25, 1931 July 14, 1931 Aug. 4, 1931 Nov. 12, 1931 Sodium thiosulphate given	1.33 1.95 0.19 0.03 0.16 0.05 0.27 0.000	.... Trace 0.151 ..... 0.073 0.269	May 14, 1931 (1) Dried specimen: 5.22 mg. old arsphenamine. (2) Tissue section: As_2S_3, granules present in epidermis, mostly in horny layer, still more abundant in corium, especially in deeper parts around blood vessels	May 21, 1931 Neoarsphenamine 1:10 +D Silver arsphenamine 1:20 + Old arsphenamine 1:20 +D
5. L. L., female, white, Italian, 23 years of age, housewife, under observation since Aug. 13, 1931	Vitiligo spots first noticed on hands in June, 1931; on admission, many spots pinhead to half-dollar size, irregularly outlined, with hyperpigmented borders on hands; similar larger spots present on flanks	Biopsy from right side: borderline of vitiligo and normal skin. Fontana stain: epidermis—pigment unevenly distributed in basal cell layer; entirely absent in some parts of section; present in prickle cells in some parts; corium—occasional chromatophores present Pathology: moderate keratosis and edema of epithelium; increase of spindle-shaped cells in corium, particularly around vessels	Aug. 13, 1931 Aug. 20, 1931 Sept. 14, 1931 Sept. 17, 1931 Oct. 2, 1931 Oct. 15, 1931 Sodium thiosulphate given	0.69 .... 0.14 .... 0.098	..... 0.62 0.13 ..... 0.375 0.000	Sept. 29, 1931 (1) Dried specimen: 0.011 mg. old arsphenamine. (2) Tissue section: occasional granules of As_2S_3 in epidermis and in papillary layer of corium	Oct. 2, 1931 Neoarsphenamine 1.10 + Silver arsphenamine 1:20 + Old arsphenamine 1:20 +
6. S. B., female, white, 9 years of age, school girl, under observation since Sept. 15, 1931	First vitiligo spots appeared about 1½ yrs. ago; irregularly outlined areas of depigmentation, dime to dollar size, on neck, right shoulder and arm; in center of larger spots, islands of normally pigmented skin	Biopsy from vitiligo spot on right shoulder. Fontana stain: pigment unevenly distributed in epidermis; scanty or absent in some parts of section, more abundant in others; in some places, absent in basal cell layer but present in prickle cell layer, no chromatophores seen in corium Pathology: slight edema of epithelium; slight atrophy of rete pegs; increase of spindle-shaped cells in upper corium and around vessels	Sept. 22, 1931 Sept. 24, 1931 Nov. 12, 1931	0.002 ..... 0.003	0.206 0.143 0.082	Oct. 8, 1931 (1) Dried specimen: biopsy inadequate. (2) Tissue section: no arsenic found	Nov. 21, 1931 Neoarsphenamine 1:10 + Silver arsphenamine 1:20 + Old arsphenamine 1:20 ±

7. C. J., female, Negro, 22 years of age, nurse, under observation since Jan. 26, 1932	Vitiligo first noticed 4 mos. ago, beginning with three pea-sized white spots on back; spots gradually increased in both size and number; now scattered extensively over neck, chest and abdomen; pinhead to half dollar size; varying degrees of depigmentation; a few discrete spots on arms and thighs	Biopsy from back: borderline of vitiligo and normal skin. Dioxyphenylalanin test: in normal part of section, numerous round cell melanoblasts in epidermis; only a few dendritic cells seen; plenty of pigment both in epidermis and in corium; at borderline, numerous dendritic melanoblasts present, some large, with long dendrites; in vitiligo part, no pigment, no melanoblasts seen in epidermis; scanty amount of pigment in corium. Fontana stain: pigment entirely absent from some areas of epidermis and subadjacent areas of cutis; in others, plenty in epidermis and upper cutis	Jan. 26, 1932 Jan. 27, 1932 Feb. 4, 1932	0.47	0.125 0.000	Jan. 26, 1932 (1) Dried specimen:* 0.000 mg. old arsphenamine. (2) Tissue section: numerous granules of As_2S_3 present in epidermis, in basal cell, in prickle cell, and horny layers; granules also present, though less numerous in papillary layer of corium and in sebaceous glands	Neoarsphenamine 1:10 ± Silver arsphenamine 1:20 +
8. McW., female white, 27 years of age, teacher, under observation since May 16, 1931	Vitiligo of 14 years' duration; white areas gradually increased in size and number until white spots now scattered over entire cutaneous surface; many large areas on trunk and extremities, with apparent increase of pigment in other places; almost entire face devoid of pigment	Biopsy from thigh: vitiligo and adjacent hyperpigmented area. (1) Dioxyphenylalanin test: in pigmented part of section, numerous melanoblasts with pale nucleus and projecting dendrites near basal cell layer; complete absence of these and of pigment in vitiliginous part of section. (2) Fontana stain: pigment ranges from complete absence in vitiliginous part of section, to large amounts in hyperpigmented part	May 19, 1931 July 2, 1931 Nov. 17, 1931 Jan. 25, 1932	0.125 0.88 0.113 0.003	....	Jan. 26, 1932 (1) Dried specimen: 0.36 mg. old arsphenamine. (2) Tissue section: As_2S_3 granules in moderate quantity are seen in epidermis and in papillary layer of corium	Not done
9. G. H., male, white, 37 years of age, manufacturer, under observation since March 13, 1930	Vitiligo of 27 years' duration; areas of hyperpigmentation appear, fade, disappear, and are succeeded by areas of depigmentation, not always confined to sites of previous brown spots; sunlight darkens hyperpigmented areas still further, but does not affect depigmented areas; entire cutaneous surface involved	Biopsy from back: vitiligo and melanoderma; uneven distribution of pigment in basal cell layer; occasional chromatophores present in corium	March 13, 1930 July 14, 1930 Nov. 14, 1930 Dec. 17, 1931 Dec. 22, 1931	1.85 0.168 0.000 0.258	.... 0.315	Dec. 22, 1931 (1) Dried specimen: 0.48 mg. old arsphenamine. (2) Tissue section: discrete granules of As_2S_3 visible in basal cell layer; occasional single granules present in corium and in subcutaneous fat tissue	Not done
10. A. R., male, white, 47 years of age, grocer, under observation from Dec. 2, 1930, to March 20, 1931	Depigmented and hyperpigmented areas scattered all over body, mostly on back, chest and extremities	Biopsy from vitiligo area (natural preparation): no pigment in basal cell layer; occasional cells filled with granular pigment in subpapillary layer Pathology: epidermis irregular, with slight hyperkeratosis in places; moderate infiltration limited to upper and midcutis, both diffuse and focal, around blood vessels, follicles and sebaceous gland. Infiltrate: small and large round cells; moderate perivascular edema	March 1, 1931	0.036	0.071	(1) Dried specimen no. 1: 0.44 mg. old arsphenamine; dried specimen no. 2: 0.39 mg. old arsphenamine. (2) Tissue section: granules of As_2S_3 present in abundance both in epidermis and in corium	Not done

* Specimen very small.

sisting of innumerable small white spots, which started from the neck and spread over the breast, thorax and back. No mention is made of any hyperpigmentation. The spots had succeeded a generalized psoriasis, which had cleared up after 1 Gm. of arsenic acid was given. The author remarks that while leukoderma following the administration of chrysarobin appears only on the sites of application of the remedy, that following the administration of arsenic may be seen also on sites hitherto exempt from psoriasis. This is equivalent to making the arsenic at least a contributory factor in the disappearance of pigment.

Even after the advent of arsphenamine, the inorganic compounds of arsenic continued to claim the great majority of reports on abnormalities of pigmentation. Stahl, writing in 1916 on arsenical keratosis and melanosis, included one personal case in which the dark melanotic background was dotted with small, sharply defined, round and irregular depigmented spots. This patient had been taking arsenic for years on account of psoriasis, and neuritis and keratosis had developed in addition to the pigmentary abnormalities.

A somewhat similar case is mentioned by Van Kerckhoff—that of a 12 year old patient with psoriasis, who had a long history of arsenical treatment, and in whom melanoderma finally developed with extensive white spotting (definitely lighter than the normal skin) on the breast, back and abdomen, sites which had hitherto been free from eruptive manifestations. Van Kerckhoff, however, considered other factors responsible and discounted the rôle of arsenic.

In May, 1930, appeared a report of a case by Jausion, Longin and Gauch: In a man who had been receiving acetarsone for malaria, a severe exfoliative dermatitis developed, followed first by extensive leukomelanoderma, and later, by a typical arsenical neuritis. The distribution of the patches of discoloration was roughly symmetrical, and the marginal zones of hyperpigmentation coincided with the most severe eruptive manifestations.

Depigmentation following the administration of arsphenamine seems to have been reported first by Buschke, in 1919. In his patient, presented before the Berlin Dermatological Society in December of that year, a generalized melanoderma had developed after the healing of a silver arsphenamine dermatitis. Scattered irregularly over the back and, more sparsely, on the chest, abdomen, arms, legs and forehead were numerous sharply circumscribed clear white spots, varying from pinhead to half-dollar size, without noticeable zones of hyperpigmentation surrounding them. The white spots spread gradually; none grew smaller. There were no subjective disturbances, and histologic examination revealed only pigment atrophy.

In 1923, Bruhns (reference 9*a*) demonstrated a patient with similar pigmentary abnormalities, associated with pea-sized depressed

atrophic spots. All these manifestations had appeared after a severe dermatitis from mixed injections of neoarsphenamine and merbaphen. A biopsy failed to throw any definite light on the pathogenesis of either the white or the atrophic spots.

The following year a case was presented by Almkvist (reference 1*a*) before the Dermatological Society in Stockholm. This patient's vitiligo, limited to the right side of the abdomen and the inguinal region, had appeared after injections of mercury and neoarsphenamine. In Birnbaum's patient, demonstrated in November, 1925, before the Silesian Dermatological Society in Breslau, vitiligo developed on the face and trunk, and later, lichen ruber planus on the legs, after the healing of an arsphenamine dermatitis. Jeanselme, Schulmann and Popoff, in 1926, described a case in which a diffuse melanoderma made its appearance shortly after a neoarsphenamine dermatitis; in the most darkly pigmented areas appeared vitiliginous spots and streaks. In this case the melanoderma was accompanied by hyperkeratosis.

Frei's case of the same year presented a peculiar form of arsphenamine melanosis resembling Bloch's "incontinentia pigmenti," and associated with vitiligo of the abdomen and scrotum. Bruhns (reference 9*b*) also demonstrated a second case in 1928: In a woman, following a generalized arsphenamine dermatitis, large plaques of vitiligo developed on the trunk and arms; they were faint at first, then gradually became more pronounced; most of the plaques were surrounded by hyperpigmented zones.

No more cases seem to have been reported until February, 1930, when there appeared the article by S. Dohi describing a case of "leukomelanoderma from salvarsan injury to the vegetative nervous system." The man, 50 years of age, when found to have a positive Wassermann reaction and dilatation of the aorta, was first given mercury and potassium iodide, and later twelve injections of arsphenamine. In this instance, as in the preceding ones, the pigmentary disturbances followed on the heels of an exfoliative dermatitis, but the vitiliginous areas appeared to be more extensive—quite the dominating feature, in fact. They were sharply defined, surrounded by zones of hyperpigmentation and scattered in geographic patterns over the scalp, trunk, right arm and thighs, the plaques being especially large on the back. Hyperpigmented spots were scattered throughout both vitiliginous and normal areas. Dohi's report is especially full in observations bearing on disturbances of the nervous system in his patient. These will be discussed more fully in a subsequent section.

More recently, Korhonen described the case of a woman in whom treatment for syphilis with neoarsphenamine and bismuth brought on a severe exfoliative dermatitis. As the dermatitis cleared up, a generalized melanoderma made its appearance, with depigmented spots

which gradually combined into polycyclic areas; these were especially thick on the upper middle of the chest, flanks, sides of the trunk and the lower extremities. In this case, as in Dohi's, there were found to be functional disturbances of the sympathetic nervous system suggestive of a constitutional weakness plus injury from arsphenamine, the combined effects of which might, in the author's opinion, account for the pigmentary disorders.

The cases summarized in the foregoing section—so far as it has been possible to judge from the authors' descriptions—all present evidence that the white areas result from a true absence or diminution of pigment and not from the inclusion of normal areas within hyperpigmented ones, the color contrast producing an optical illusion. It is possible that the case reported by O'Donovan in 1925, may also fall within this category: A 50-year old box-maker, with a history of syphilis at 17, received eleven doses of neoarsphenamine (up to 0.6 Gm.) for a recurrent positive Wassermann reaction. A severe exfoliative dermatitis followed, and healing, left a blotchy pigmentation, which grew very dark, over the entire trunk, arms, forearms and upper part of the thighs. The face, legs, hands, feet and mucous membranes remained free. In the inguinal and axillary flexures, the melanoderma was most uniform, but elsewhere were numerous discrete and confluent areas, circular or nearly so, of sharply defined "white skin," from 1 cm. upward in diameter. These are likened to the raindrop leukoderma colli of secondary syphilis, except that they were larger. However, in the absence of histologic examination, or even of any definitely stated clinical comparison with the nonmelanotic areas, one is left in doubt as to the nature of the "white spots."

Among the numerous cases of melanosis from chronic arsenical poisoning reported in detail by Geyer from the mining districts of Silesia, one finds repeated mention of light-colored spots (*hellere Flecken, weissliche Flecken, leukodermartige Flecken, hellen pigmentärmeren Bezirke*), but these are shown to consist of certain vascular or papillary areas which had remained free from the general hyperpigmentation. There was no macroscopic evidence of pigment displacement, and zones devoid of pigment were never found in any of the microscopic sections examined.

A similar condition which might easily pass for vitiligo is illustrated in the case reported by Goubeau in 1913. The patient, a man of 20, had had a short but intensive course of arsphenamine and mercury for primary syphilis, followed by more or less regular treatment with hectine and hectargyre during a two year sojourn in the tropics. There had been no further manifestations of syphilis, but the man returned to France with an eruption in the throat, accompanied by a burning sensation and a bitter garlic taste. Exposed parts of the skin were deeply bronzed by the tropical sun, with the exception of certain areas

of the face and neck. Spreading over the face, in geographic patterns, were what appeared to be vitiligo plaques, and on the neck similar but smaller elliptoid white spots, with slightly marked borders of hyperpigmentation. The supposed vitiligo, however, proved to be identical in color and texture with the normal skin of the parts not exposed to the sun. When arsenic was discontinued, the throat and mouth symptoms quickly disappeared, and the color contrasts were gradually becoming less marked. Goubeau called the condition "dyschromie vitiligoïde par arsenicisme." This in turn is strongly suggestive of the "solar leukodermas" reported in increasing numbers in recent years, and raises the question whether original vitiligoid patches might not have been merely rendered visible by the excessive tanning, even without the arsenic.

If vitiligoid conditions like the foregoing are not always easy to distinguish clinically from true vitiligo, the actual degree of pigment loss or displacement in any depigmented area is a matter of still greater uncertainty, and can, strictly speaking, be determined only by microscopic examination. Many case reports lacking such confirmation must be interpreted with reservations. Of the fifteen cases of clinical depigmentation under consideration here, only three contain biopsy reports. Buschke found "pigment atrophy," with slight inflammatory infiltration in the papillae, but nothing suggesting tissue changes. Frei's case showed pigment absent from the epidermis, but present in the cutis. In the Dreysel specimens, the horny layer was entirely devoid of pigment, and the rete contained only traces, and that in the lowermost layers; there was plenty of pigment in the cutis, and no considerable infiltration—only occasional small groups of cells. Bruhns' biopsy failed to throw any definite light on the pathogenesis of either the white or the atrophic spots. Details are not given. Van Kerckhoff did not report a biopsy on his patient, but stated explicitly that the white spots, though definitely lighter than the normal skin, represent only a "hypopigmentation" (*keine vollständige Leukodermia*). No tests with the dopa reaction seem to have been carried out on any of the foregoing specimens.

In regard to the cases showing a definite and marked loss of pigment, another question presents itself. It is well known that depigmentation, usually accompanied by atrophy or scarring, may follow various dermatoses, such as psoriasis, parapsoriasis, ulcerating syphilids, pityriasis rosea, microsporia, lichen simplex and lichen planus, although after some of these, hyperpigmentation is the rule and hypopigmentation the exception. Most writers attempt to distinguish true vitiligo from the aforementioned postlesional achromias. In so doing, two factors must be taken into consideration: (1) the presence and extent of atrophic changes, and (2) whether or not the achromic areas coincide in location

and outline with the original lesions. The scar with marked sclerotic and atrophic changes offers little or no diagnostic difficulty; but there are others the surface of which becomes so soft and smooth as to be identical in texture, as well as color, with that of typical vitiligo plaques, while retaining the exact configuration of the lesions which they succeeded. Langer claimed that the presence of the pilomotor reflex will identify vitiligo in such instances, its absence indicating scar tissue.

If differences in texture are not always easy to detect, it is often still more difficult to determine whether the depigmented areas correspond to the sites of previous eruptive manifestations, or have formed independently of such lesions. It is estimated that only a small part of syphilitic leukoderma is secondary to manifest syphilitic lesions, the majority of cases representing a primary morbid entity. Rille and others have observed leukoderma originating by involution of primary psoriasis plaques; on the other hand, Van Kerckhoff has repeatedly found varying degrees of hypopigmentation in patients with psoriasis on parts never invaded by eruption. Of parapsoriasis, Almkvist (reference 1 *b*) wrote:

> Most authors agree that leukoderma in parapsoriasis forms on the site of the cured eruption, but Langer seems to admit the existence (as in syphilis) of leukodermic patches of other origin.

Sometimes the dermatosis appears merely to aid in localizing the vitiligo. Thibierge has described the process as observed in tertiary syphilis: An ulcerating syphilid leaves a scar, more or less irregular, with a surrounding zone of hyperpigmentation. By repetition and extension of this process, considerable areas of hyperpigmentation result, and these in turn become invaded by rounded areas of depigmentation, the latter without having been preceded by ulcerations or by any appreciable change in the skin. Thus, a generalized vitiligo may result, having originated in the limited region of an ulcerating syphilid.

Of the cases under consideration here in which arsenic was known to have been administered, the first three are open to question as being possible residues from a previous dermatosis. The Dreysel case is listed by Lindberg as one of depigmentation following lichen planus. Dreysel admitted that some of the white spots were slightly suggestive of atrophic changes, but asserted that no such changes were found in the microscopic sections. However, his data on the location of individual spots are not precise enough to exclude the possibility of their having succeeded older lichen nodules. The residue of both white and brown spots here would then be comparable to the simultaneous occurrence of leukoderma psoriaticum and hyperpigmentation from healing psoriasis plaques of the same person. Roscher's case comes under suspicion on account of the dermatosis for which the arsenic was originally administered. As already indicated, observers present at the demonstration

of this patient were inclined to attribute the depigmentation to the original dermatosis. Details are lacking in regard to the precise location of the latter. Stahl's case was complicated by a psoriasis of many years' standing. Obviously in all such cases only the most careful and constant observation on the part of both physician and patient could establish or exclude a direct relationship between the sites of the psoriatic eruption and subsequent areas of depigmentation. Unfortunately, such data are lacking in Stahl's report, as in the great majority. Van Kerckhoff was able to state definitely that the white spots seen on his patient with psoriasis appeared where there had been no previous eruption. A second photograph taken two years later shows eruptive manifestations beginning around the borders of the still existent, sharply defined leukodermic spots.

The foregoing cases may be taken as representative of a considerable number in the literature of depigmentation following dermatoses treated with arsenic, in which the question remains open whether (1) the depigmentation is a relic of the dermatosis and has nothing to do with the arsenic, or (2) the depigmentation is due to the arsenic and has nothing to do with the dermatosis, or (3) the depigmentation is localized in its initial stages by the dermatosis (as in Thibierge's example of the tertiary syphilid) but is essentially due to some other factor, possibly arsenic. As mentioned previously, Rosenthal pointed out that depigmentation following arsenical therapy may be seen on sites hitherto exempt from psoriasis. The evidence would seem to indicate that arsenical treatment for various dermatoses may be followed by depigmentation occurring independently of the dermatosis, and that arsenic should therefore be taken into account as a possible factor in such cases. However, the overwhelming majority of reports which we have been able to examine do not present data of sufficient precision to exclude the dermatosis as a causal or at least a localizing factor.

In none of our own cases had any circumscribed skin lesions preceded the vitiligo in situ. Only one of the ten patients had a definite history of syphilis (case 3, chancre twenty-five years previously) and none showed any clinical manifestations of the disease while under our observation. Two of the patients (cases 2 and 3) received arsphenamines on account of recent positive Wassermann reactions; a third (case 1) showed a negative Wassermann reaction but was syphilophobic. All ten patients had negative Wassermann reactions during the development of the pigmentary changes, and the tests have remained so to date. In this connection it is interesting to note that Hashimoto, among 153 unselected cases of vitiligo, did not find a single one in which there were clinical manifestations of syphilis, and only 3 of 63 cases in which there was a positive Wassermann reaction. While this does not prove

that vitiligo is never due to syphilis, it should dispel any lingering remnants of the once popular myth that vitiligo is a tell-tale sign of a previous syphilitic infection.

EFFECTS OF ARSENICAL DERMATITIS ON PIGMENTATION; ARSPHENAMINES VS. OTHER COMPOUNDS OF ARSENIC: HISTOLOGY

Depigmentation following arsphenamine therapy was in every instance preceded by a generalized exfoliative dermatitis. This arsphenamine dermatitis is considered by Boutelier and some others to be merely another example of the inflammatory skin lesion which may be succeeded by pigmentary disturbances. The arsenic would here be responsible in either case, whether directly or indirectly. There is, of course, no question of scarring here, for the process is diffuse, and after healing, with desquamation, leaves the skin uniformly soft and smooth. To all appearances, only the pigment function remains impaired.

It might be expected that a study of the dermatitis lesions would furnish some clues to the disappearance of pigment. This does not seem to have been the case. Histologic examinations of the skin of patients with arsphenamine dermatitis have been reported but rarely. By far the most complete picture of the process in evolution is given by Kyrle (reference 29 b), and will be taken up later in conjunction with our own cases. Kyrle, however, is practically silent on the question of pigment in this connection, while the few remaining reports available are more or less contradictory, besides being open to one objection or another: Thus Bergmann, reporting a fixed tuberous exanthem following injections of arsphenamine, described inflammatory changes in the cutis, but gave no data on the epidermis. As this patient had no desquamation, nor any generalized pigmentary disturbance, the case is not typical. Buschke and Freymann reported biopsies from two patients in whom a lichen ruber-like exanthem developed from neoarsphenamine, while Heller has reported the pathologic changes in a dermatitis following the administration of arsphenamine and neoarsphenamine. In both the latter instances the patients had received mercury and a solution of potassium arsenite in addition to the arsphenamines; thus the rôle of any one drug in producing the lesions was obscured. In Heller's case there was, furthermore, a generalized hyperkeratosis which clinically overshadowed the dermatitis at the time the biopsy was taken. Moser (reported by Jaffé) gives histologic findings in two cases of generalized exfoliative dermatitis from sulphoxylate arsphenamine, both terminating fatally, but pigment is not mentioned.

So far as these reports are comparable, there seems to be little visible impairment of the lower epidermal (i. e., pigment-forming) cells,

save in the Moser specimens. One finds, for example, "suggestions of a thinning of the prickle-cell layer" and "prickle-cell layer scarcely changed—at least not thinned" (Buschke and Freymann's cases), and "no essential changes in the rete" (Heller). Bergmann gives no data on epidermal changes seen in his biopsy. In general, slight broadening of the granular layer and abnormal cornification constitute the chief changes observed in the epidermis, and even these are totally lacking in uniformity. Thus, of the two Moser specimens, both taken from patients with terminal lesions from the same drug, one showed extensive cornification, in some places extending all the way to the basal layer, while in the other, the horny layer was greatly thinned and retained cells with nuclei (parakeratosis). In the second Moser specimen, the entire epidermis was thinned out in many places, especially over the papillae; but the rete pegs, on the contrary, were often greatly lengthened, and in parts, widened. The most striking change was a vascular degeneration. Three of the remaining cases showed a marked follicular keratosis, accompanied by hyperpigmentation (Buschke and Freymann; Heller). It is possibly significant that all three of these patients had received inorganic arsenic in addition to an arsphenamine.

In all the foregoing cases the cutis was reported as showing perivascular infiltration, especially in the subpapillary layers. In all but Heller's case (in which the keratosis was more marked than the dermatitis) this was described as intense, and in one (Buschke and Freymann) there were also extensive hemorrhagic areas in the subcutis. Most specimens showed cellular infiltrates around the sweat glands. Edema was not a constant finding, but in some sections, notably Moser's, was very marked; here the collagenous fibers were loose, swollen and spread apart, leaving hollow spaces. Abnormal deposits of pigment, where mentioned, were chiefly in the papillary layer.

There is no mention of any depigmentation following the dermatitis in any of the foregoing cases. Of the three in which melanoderma developed, Heller's (the only one in which pigment findings are described in any detail) showed the pigment to lie almost exclusively in the cutis. It was abundant in the papillary and reticular layers, and especially in the tips of the papillae, where it appeared to be piled up in extracellular heaps, although some was also present inside the cells.

Let us examine for a moment one of the few reports available on histologic changes in dermatitis with subsequent pigmentation from arsenic other than the arsphenamines. Brooke and Roberts, writing of the epidemic of arsenical beer poisoning in 1901, described the bulk of the skin changes as being confined to the epidermis. The cutis is reported as practically unaltered. There was some congestion of vessels, which were surrounded by a mantle of wandering cells, but leukocytosis

—in the sense of collections of cells in particular areas—was "conspicuous for its absence." On the other hand, the stratum lucidum, the stratum granulosum and the rete were at first hypertrophied; later, they degenerated and became atrophied, coincidentally with a thickening of the horny layer. The great preponderance of pigment here was found in the epidermis. The basal cells undergoing degeneration were filled with amorphous pigment granules. Some connective tissue cells close below the epidermis also contained pigment, but there was no general pigmentation of the cutis, not even of the upper layers.

The latter report is illuminating for the picture of what may happen in normal persons. Too often the condition for which arsenic was administered obscures the picture. Gans, for example, found degenerative changes in both the epidermis and the cutis, in his study of a case of arsenical melanosis; but these findings are compromised by the persistence of lesions of dermatitis herpetiformis, for which the arsenic ("both injection and Fowler's solution") was originally administered.

From the cases of dermatitis so far examined, one might be tempted to conclude that the arsphenamines attack primarily the cutis and its vascular structures, while the inorganic arsenicals do their principal damage in the epidermis. Accumulations of pigment would also appear to localize themselves in the structures subject to greatest inflammatory or degenerative change, being found principally in the cutis in the cases of arsphenamine dermatitis and in the epidermis in the Brooke-Roberts' cases of beer poisoning.*

Osborne drew somewhat similar conclusions from his studies of arsenic as revealed in microscopic examinations of tissue sections from patients with arsenical pigmentation and keratosis (1925) and arsenical dermatitis (1928). In his specimens from cases of arsphenamine dermatitis, he found the bulk of the arsenic deposited deep in the corium around the arterioles and capillaries, in the walls and lumen of the sweat and sebaceous glands and their ducts, and in the hair follicles and shafts. Sections of normal skin from patients receiving arsphenamines showed arsenic in the same locations but in relatively small amounts. At no stage of the dermatitis could any but the most minute quantity of arsenic be found in the epidermis, including the horny layer. The subpapillary layer was almost entirely free from arsenic, and although special search was made around the capillary loops in the papillae, only trifling amounts were seen there. On the other hand, in melanosis and keratosis from solutions of potassium arsenite and of arsenous and mercuric iodide, U. S. P., the arsenic was reported to be localized chiefly in the epidermis, although plentiful also in the upper corium, and in the sebaceous glands

* Brooke and Roberts, for reasons which they give, assume that the arsenic entered the system in the form of arsenates.

and their ducts. The distribution of the arsenic, however, did not bear any apparent relation to the distribution of pigment. Arsenic was present whether pigment was present or not, and was separate and distinct from the pigment.

So far, we do not find the evidence sufficient for the distinction already suggested between the action of the arsphenamines and that of the other compounds of arsenic. In our own specimens, as will be seen presently, we found arsenic from both sources distributed indifferently throughout both epidermis and cutis; and pathologic changes in specimens from cases of arsphenamine dermatitis, far from being confined chiefly to the cutis, were, if anything, more pronounced in the epidermis. Clinically, all forms of eruptions—scarlatiniform, lichenoid, eczematoid—as well as hyperkeratosis and melanoderma have been reported due to arsenic from the most varied sources, including arsphenamine medication. Moreover, on a single patient, examined at different stages, one may observe all the gradations between a simple erythematous rash and a severe vesicular dermatitis with grave constitutional symptoms. The pathologist's view is perforce a snapshot, not a moving picture; and he will be limited, not only in time, but also in space, for of all the multitude of constantly changing skin manifestations seen by the clinician, comparatively few will come within range of his camera. Thus, if the changes so far reported in the cases of arsphenamine dermatitis appear to be mostly in the cutis, the clinical descriptions (where available) suggest at once that this is so, either because the dermatitis had not yet progressed beyond the early inflammatory stage or had receded until only vestiges of inflammation remained, or because the eruption took the form of a lichen planus, for example, rather than of a pityriasis or a vesicular eczema. Hence, while positive findings under the microscope are always worthy of consideration, negative ones, especially in view of the small number of reports available for comparison in the present instance, are not necessarily significant. With the many cases of melanosis combined with hyperkeratosis but without eruptive manifestations reported frequently in patients taking arsenic by mouth, we are not concerned here.

ARSENICAL DERMATITIS AND VITILIGO: ARSENIC FINDINGS IN BLOOD, URINE AND SKIN

None of the foregoing reports has taken up the question of depigmentation, either in relation to inflammatory changes or to the presence of arsenic in the tissues. In our own cases, we were able to verify, in the same patients, not only the disappearance of pigment from the epidermis immediately following an arsenical dermatitis, but also the pres-

ence of arsenic granules in the skin, during both the inflammatory stage and the subsequent pigmentary changes.

Taking first the three cases of exfoliative dermatitis following arsphenamine medication: As the dermatitis subsided we watched snow-white vitiligo spots appear and spread; contrasting with these, there also developed, in each instance, a hyperpigmentation of surrounding areas, sometimes spotted or annular, sometimes diffuse (figs. 4, 5 and 7). That the white spots were definitely vitiligo and not due to color con-

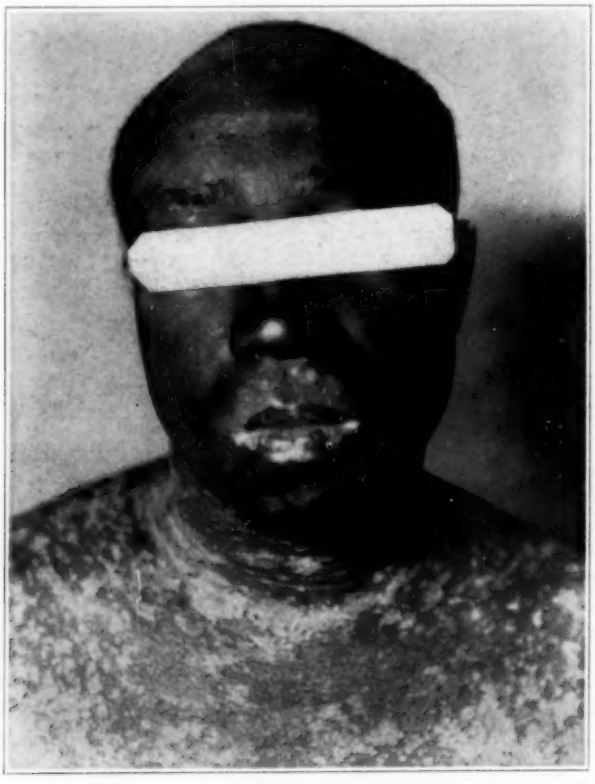

Fig. 4 (case 1).—Depigmented and hyperpigmented spots on the chin and mucous membranes of the lip following arsphenamine dermatitis.

trast alone is demonstrated by our findings in the skin sections examined for pigment. Both the Fontana stain and the dioxyphenylalanin test showed the epidermis of the vitiliginous parts to be devoid of pigment except in biopsies taken after repigmentation had begun. In the latter (cases 2 and 3), the dioxyphenylalanin test brought out the presence of dendritic melanoblasts loaded with pigment, in or near the basal layer of the epidermis. In all cases pigment was seen in the chromato-

phores of the corium, although in case 1 only a few scattered chromatophores were visible, and those were seen in the lowermost part. There was pigment both within the cells and free in the lymph spaces, with a tendency to clumping around the blood vessels and hair follicles.

The pigment findings in the hyperpigmented sections were typical of melanoderma; the specimens tested with dioxyphenylalanin especially revealed active pigment formation in the basal cell layer, and even the natural preparations showed an abundance of melanin in the lower

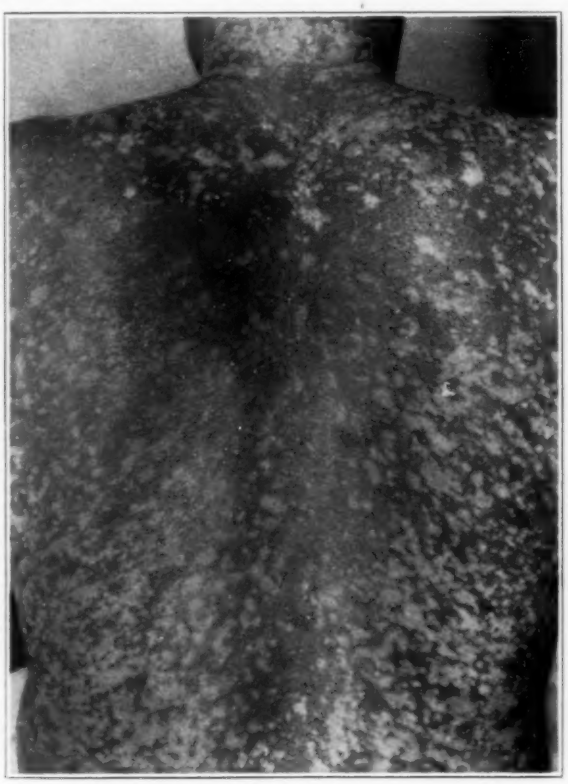

Fig. 5 (case 1).—Posterior view of the same patient, showing the vitiliginous areas.

part of the epidermis and in the upper portions of the cutis. In transitional zones, including hyperpigmented, normal and vitiliginous areas, there was a gradual diminution of epidermal pigment to complete absence in the vitiligo part of the section, although chromatophores could be seen in the upper corium in all parts of the section (figs. 9-12).

The tissue changes which preceded or accompanied these pigmentary changes were not limited to inflammatory signs in the cutis, as in most of the cases of arsphenamine dermatitis previously examined. The

epidermis in all our cases was markedly thickened and irregular. This was due not only to disturbances of keratinization (both hyperkeratosis and parakeratosis, together with occasional broadening of the granular layer), but also to marked changes in the rete: acanthosis, disorganization of the basal cell layer and granular degeneration. In some sections there was a moderate interstitial edema.

In view of the foregoing histologic changes, we were not surprised to find visible contemporaneous evidence of the presence of arsenic in the tissues. In sections of the skin taken from all the patients under discussion, whether in the stage of active dermatitis or of subsequent pigmentation or depigmentation, we found typical granules of arsenic trisulphide. In most of the sections, the granules were scattered in considerable amounts throughout the epidermis, including the horny layer,

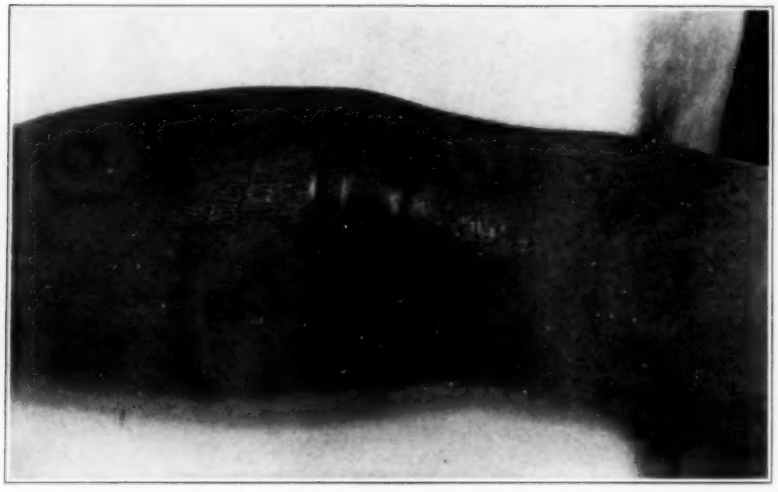

Fig. 6 (case 1).—Arsenical dermatitis at the site of infiltration around the vein.

and in the papillary layer of the corium, especially around the capillaries. Moderate amounts were also seen in the lumen of the sweat and sebaceous glands and their ducts (figs. 13-15). One patient (case 2) gave no evidence of arsenic in the epidermis in the first tissue specimen examined, though occasional granules could be seen in the corium, and microchemical analysis of a dried specimen from the same biopsy yielded 0.07 mg. of metallic arsenic. Tissue sections of a later biopsy from this same patient showed arsenic in considerable amounts in the epidermis, including the horny layer.* Case 1 showed still higher

* In preparing our tissue sections for microscopic examination, we used Osborne's modification of the Justus-Brünauer method, whereby arsenic, if present, will appear as bluish-gray crystals or granules of arsenic trisulphide. The analyses of the dried specimens were made by Dr. E. Maechling, using the Maechling-Flinn colorimetric method.

amounts of arsenic in the two dried specimens of skin—0.29 and 0.55 mg., respectively. Curiously enough, although the second dried specimen indicates an increase over that from the earlier biopsy, sections from the same (second) biopsy examined under the microscope showed fewer arsenic granules than the earlier specimens. This might well signify nothing more than an irregular distribution of the metal throughout the skin, even in closely adjacent areas, possibly contingent on the vascular supply and the cut of the section, whether straight or

Fig. 7 (case 2).—Depigmented and hyperpigmented areas, with reappearance of pigment in the white spots.

oblique. This would account not only for the apparent decrease in granules visible in a particular tissue section, but also for the higher amount reported from the dried specimen, since the latter perforce includes any arsenic present in the blood as well as in the tissue proper.

As may be seen from the accompanying charts, all three of these patients evidenced retention of arsenic not only in the skin, but also in blood and urine for considerable periods after arsphenamine medication had been stopped. While the precise mechanism of storage and elimi-

nation is still unknown, it has been shown that in the great majority of cases the bulk of the arsenic is eliminated within the first week after intravenous injection. The amounts still to be considered within "normal" limits have been variously estimated as ranging up to 0.05 mg. per hundred grams of dried specimen (either blood or urine) for persons not under treatment with the arsenicals, and up to 0.4 mg. per hundred grams of dried specimen for patients under neoarsphenamine medication (Bering; Cannon, Myers, Karelitz and Maechling). The repeated finding of considerable amounts after long periods, in conjunction with clinical symptoms of intolerance, can reasonably be

Fig. 8 (case 4).—Vitiligo in a patient without history of arsenic intake.

adjudged more than a mere coincidence. One patient, for example, (case 3), showed 1.61 mg. of arsenic in the blood and 1.011 mg. in the urine more than three months after the last injection of arsphenamine. His dermatitis had not yet entirely healed at this time, and pigmentary changes were already beginning. Another patient (case 2) showed over 3 mg. of arsenic in her urine five months after readmission to the clinic for an arsenical dermatitis. This was more than seven months after the last injection of neoarsphenamine. At this time, as can be seen from chart and case report, the dermatitis had cleared up, but the pigmentary changes were in full progress. Subsequent gradual decreases in the arsenic in the blood and urine of all three patients roughly paralleled the disappearance of the vitiligo, although there were individual variations which baffled analysis. In cases 1 and 3, sodium thiosulphate

seemed to hasten elimination of the arsenic, but in case 2 the highest peaks of arsenic in the blood and urine occurred from one to five months after the injections of sodium thiosulphate had been stopped.

The question may be raised whether bismuth does not share with arsenic the responsibility for the cutaneous disturbances, since two of the three patients had received bismuth in addition to an arsphenamine. Here we can only say that all three patients later tolerated bismuth, or

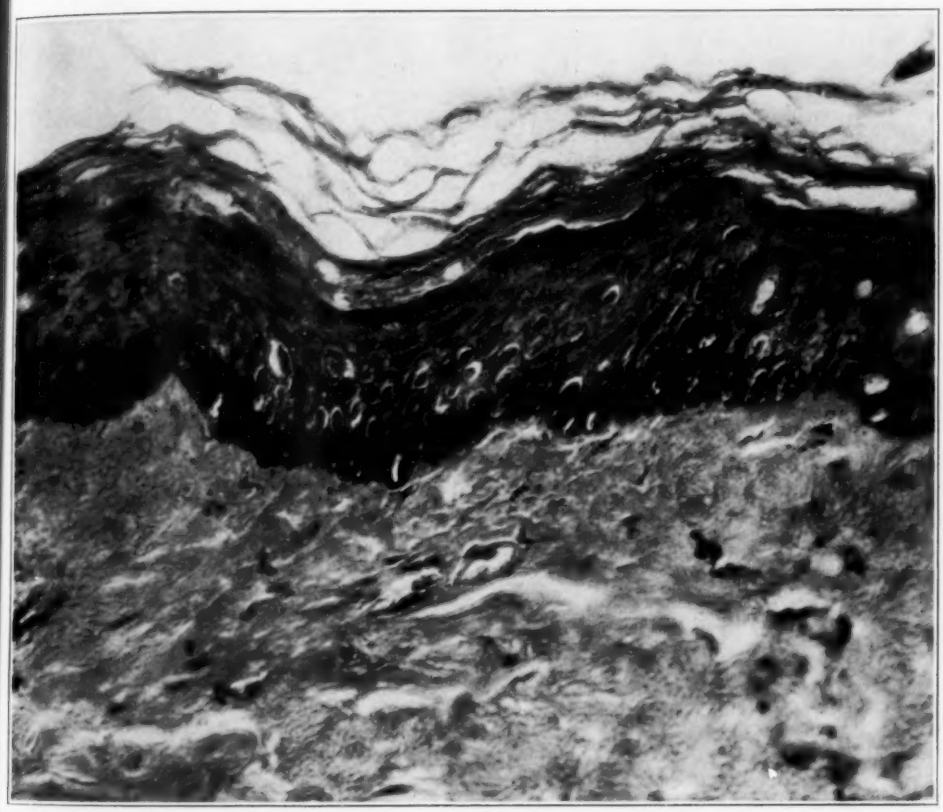

Fig. 9 (case 2).—Section of a shoe-black spot, showing enormous accumulation of pigment in the basal cell layer of the epidermis. Routine stain (hematoxylin-eosin); × 225.

mercury, or both, and that the vitiligo steadily diminished in extent and intensity during this time.

In our second group of cases (those of vitiligo not preceded by dermatitis, and without any definite history of arsenic other than the laboratory findings), examinations for pigment revealed substantially the same picture as in the cases of arsphenamine dermatitis, both sections stained by the Fontana method and others tested with dioxyphenylalanin

confirming the loss of pigment indicated by the clinical picture. In all the latter cases, pathologic changes other than loss of pigment were either lacking or not sufficient to account visibly for such serious derangement of the pigment function. Examinations of the skin of these patients for arsenic in most instances revealed even larger quantities than were found in the cases of arsphenamine dermatitis. The first patient in this group (case 4) showed 5.22 mg. of metallic arsenic per hundred grams

Fig. 10 (case 2).—Section of vitiliginous skin, showing complete absence of pigment in the epidermis. Routine stain (hematoxylin-eosin); × 175.

of dried specimen, the largest quantity we ever found in a section of human skin (figs. 8 and 15). Specimens of blood and urine from this patient yielded correspondingly high percentages of arsenic, as may be seen from the table. The source of this intake could not be determined with any degree of certainty, although all patients were carefully questioned concerning occupation, living conditions, food and previous medication. For data on the various possibilities for incidental intake of arsenic, one may consult Myers and Cornwall.

In the matter of localization of the arsenic (whether dermal or epidermal), we were unable to detect any uniform difference between the cases of arsphenamine dermatitis and the ones in which (presumably) arsenic was obtained in other forms. While there were individual variations in quantity and distribution of the granules, in both groups of cases substantial amounts were observed in the epidermis (all layers) as well as in the corium, both superficial and deeper parts (figs. 13-15). It was, of course, impossible to differentiate microscopically in the tissues the different classes of arsenic compounds, since by the method used, arsenic, whether organic or inorganic, pentavalent or trivalent, would be reduced to the trisulphide. Irrespective of its primary point

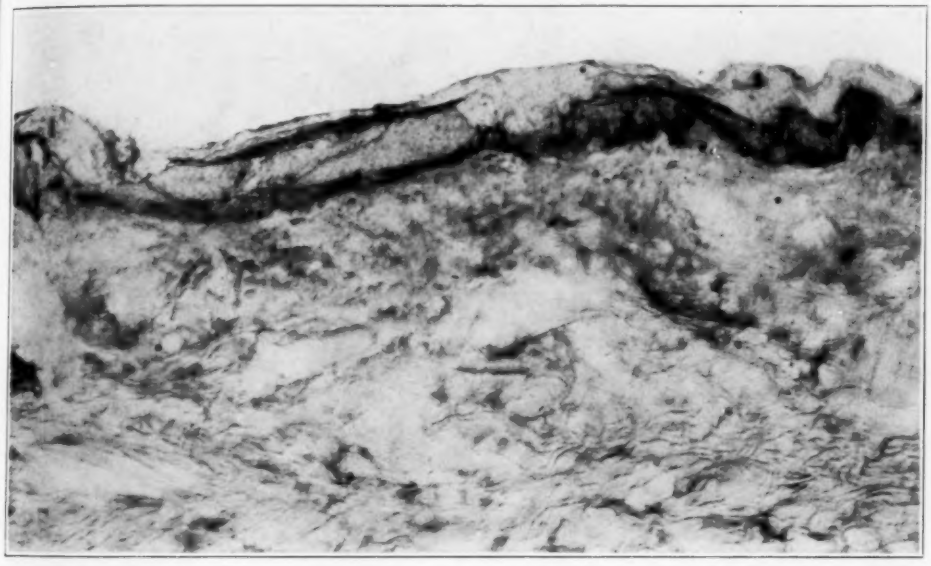

Fig. 11 (case 7).—Dopa reaction. Borderline between normal and vitiliginous parts of skin. The round cell melanoblasts in the normal part of the skin to the right become larger, with numerous processes, as they approach the vitiliginous part, then disappear entirely; × 150.

of attack, the arsenic present would seem to furnish ample cause for direct injury to the vital portions of the skin, with consequent impairment of the pigment-forming function. That arsenic was found independently of the presence or absence of pigment is not surprising, as the initial damage to the cells is undoubtedly done before any signs of structural change can be detected with the means now at our disposal.

ARSENIC METABOLISM AND LOSS OF PIGMENT FUNCTION: MECHANISM

How these changes take place can only be a matter for conjecture until more is known in regard to both the metabolism of arsenic in the

body and the normal processes of pigment formation. Many writers have attempted to explain arsenical melanosis by a speeding up of the natural rhythm of oxygen exchange by the arsenic deposited in the tissues; in the skin, this would hasten the oxidation of certain colorless premelanins to the finished melanin. Depigmentation would then result from premature exhaustion of the epidermal cells.

According to Bloch, the immediate precursor of melanin is probably di-hydroxyphenylalanin, which the basal cells of the epidermis, the

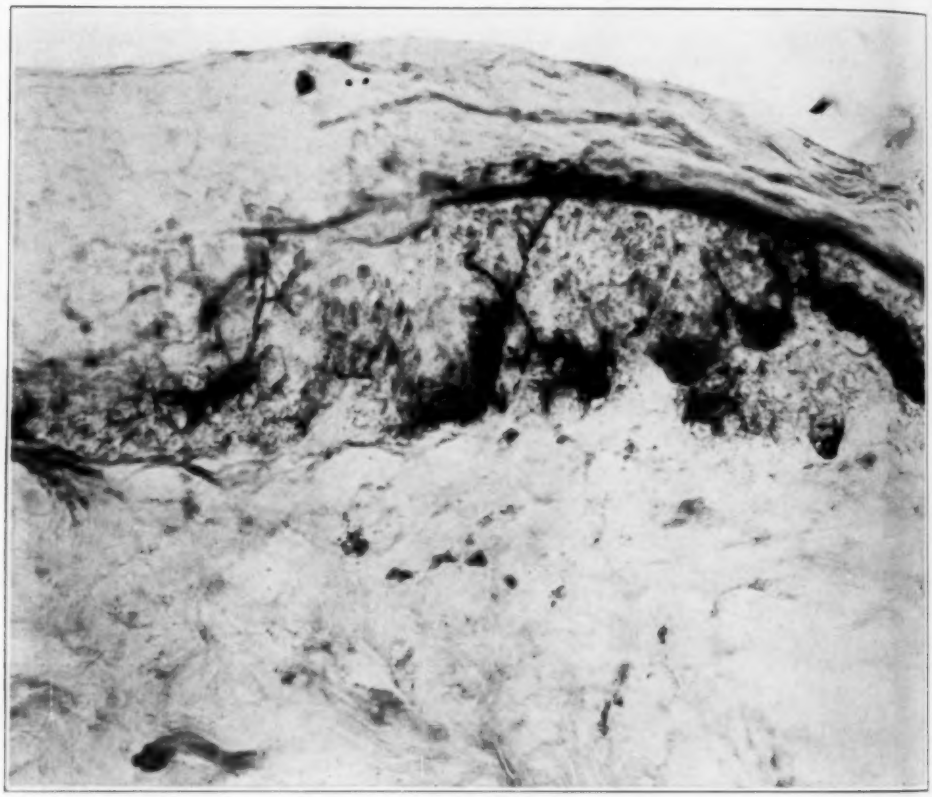

Fig. 12 (case 7).—Same section as in figure 11; dopa reaction. Note the round cell melanoblasts at the right of the section, and melanoblasts with their numerous branching processes; × 600.

melanoblasts, by virtue of a specific oxydase, di-hydroxyphenylalanin oxydase, convert into the finished pigment. The activity of arsenic has been conceived, even as early as 1879, by Binz and Schulz as a reduction, by the tissues, of pentavalent forms to trivalent ones, and an oxidation of trivalent forms to pentavalent ones. The therapeutic action of the asphenamines has been likewise attributed to their conversion into the higher oxides as or before they enter into combination with

the cellular proteins. Interplay of these factors forms the basis for most of the various attempts to explain pigmentary abnormalities following arsenic. Boutelier, for example, has suggested that in the breaking up of the arsphenamine molecule, the setting free of the phenol group furnishes a melanogen more sensitive to oxydases than is normally produced.

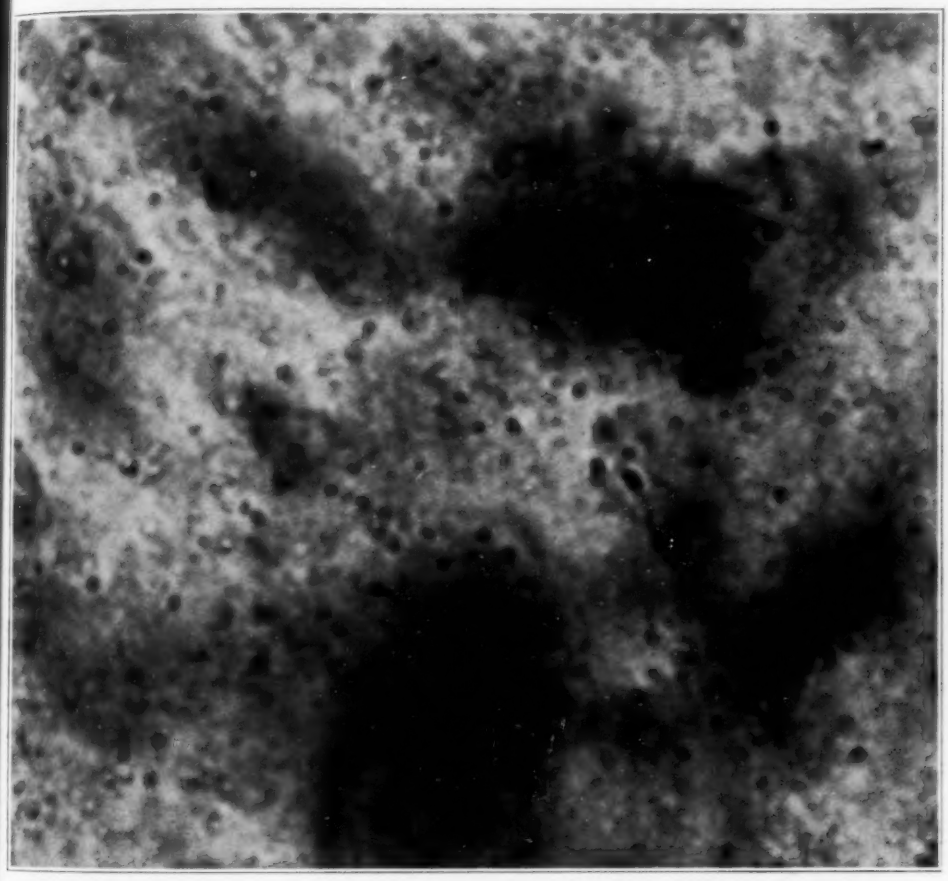

Fig. 13 (case 1).—Photomicrograph showing granules of arsenic in the corium; × 2,000.

At all events, the epidermal cells evidently possess some property of reacting specifically to the arsphenamines. As long as this reaction is adequate for the metabolism of the arsphenamine molecule, an equilibrium is maintained between the stimulus and the response of the various cell functions. As soon as this equilibrium is disturbed, either by an excess of arsenic to metabolize or by some primary inadequacy of the cells themselves, functional disturbances set in. The order of

events is differently conceived by different observers. Many think the arsphenamines attack primarily the vascular structures of the cutis, penetrating to the epidermis only when the latter is already injured by some other agent, as syphilitic toxins. According to Kyrle (reference 29 *b*), however, who made multiple thorough and painstaking histologic examinations of specimens from patients in various stages of arsphena-

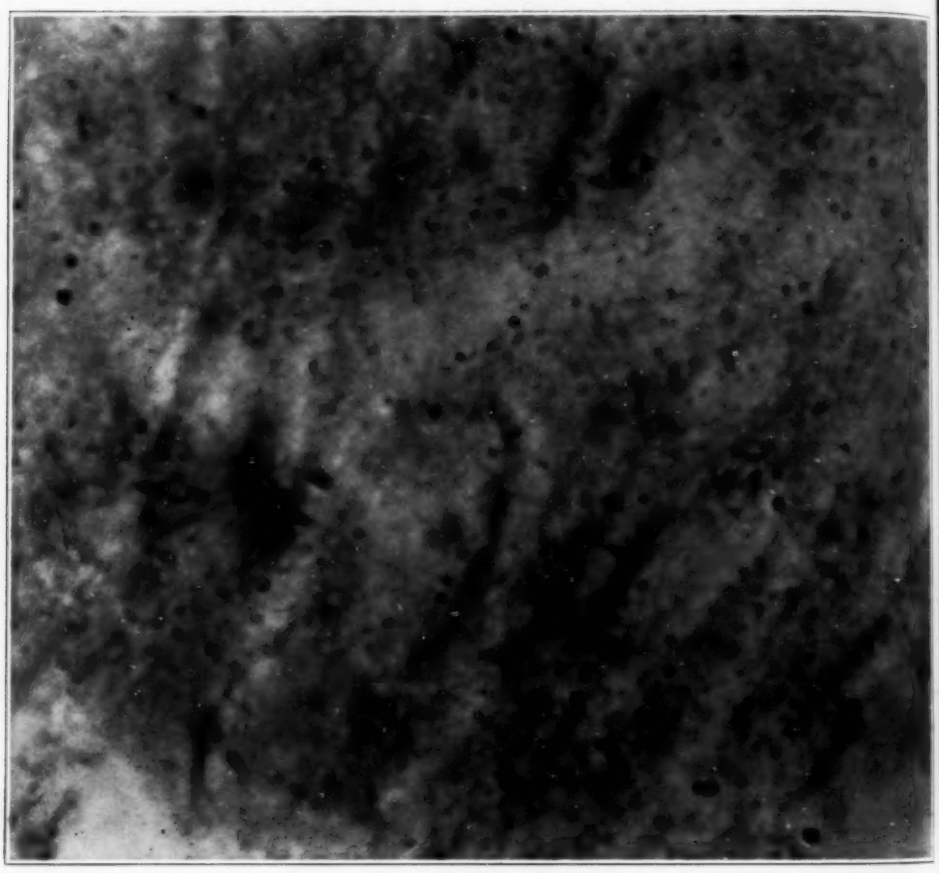

Fig. 14 (case 10).—Photomicrograph showing granules of arsenic throughout the epidermis in vitiligo section.

mine dermatitis, the primary point of attack is in the epidermis. The first functional disturbance of the epidermal cells causes an irritation of the sensory nerve fibers, producing a reflex stimulation of the vasomotor mechanism. It is the latter which furnishes the basis for inflammatory phenomena in the cutis. The cutis at first shows in the papillary and reticular layers only a dilatation of blood vessels and a scanty infiltration consisting chiefly of lymphocytes. Clinically, this is manifested by

an erythema. At this stage, no changes are as yet discernible in the epidermis, though it can scarcely be doubted that structural changes accompany functional ones—one merely does not perceive the initial steps, which are masked by later and more striking changes. This erythema, then, represents an effort to reestablish functional equilibrium by means of an active hyperemia and may be only transitory, in which case the symptoms recede and a true dermatitis does not develop. If the irritation is continued, however, more serious changes occur in the epi-

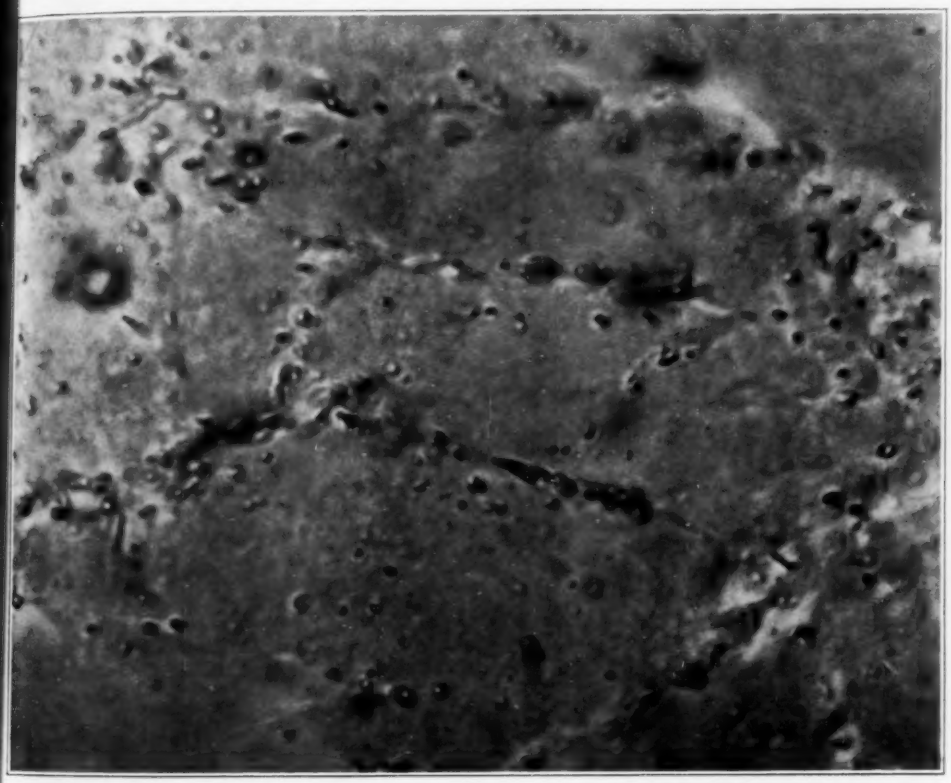

Fig. 15 (case 4).—Photomicrograph showing enormous quantity of arsenic granules in the cutis. This patient showed 5.22 mg. of metallic arsenic per hundred grams of dried specimen; × 1,200.

dermal cells, imperceptible at first, but leading gradually to a breaking down of the normal structure of both cytoplasm and nucleus, with colliquation and swelling; the cells assume a globular form, and by increasing pressure are pushed out of their palisade-like alinement; in short, there is the appearance of the "status spongiosus" described by Unna. Here and there one finds at this stage indications of parakeratosis. The simultaneously increasing irritation of the vasomotor mechanism

leads eventually to passive hyperemia and stasis, with exudation of serum and further infiltration of cells into the cutis. These in turn accentuate the degenerative processes already begun in the epidermis, which now shows the characteristic "balloon cells" of Unna. Amitotic division of these results in the formation of multinuclear giant cells. Vesicle formation is secondary, the degeneration of malpighian cells here and there leaving clefts—the loci minoris resistentiae—into which pour more serous exudates from the cutis. Further invasion of round cells and leukocytes from the cutis and continued breakdown of epidermal cells lead to pustule formation. This stage is not infrequently complicated by secondary infection. Although our own cases of arsphenamine dermatitis did not show vesicle or pustule formation while under our observation, the evolution of the dermatitis, as visualized by Kyrle, is in harmony with our own findings, and provides in itself ample cause for a disruption of the normal processes of pigmentation.

Why do some persons have vitiligo after an arsphenamine dermatitis, while others do not? Why in some instances (witness our second group of cases) should arsenic, though present in surprising quantities in both skin and body fluids, be associated with few visible skin changes other than depigmentation? Similarly perplexing is the observation that the same dermatosis may leave in its wake a hyperpigmentation in one person and a hypopigmentation in another. Again, on the same person, a dermatosis may heal leaving certain sites hyperpigmented and others depigmented (Langer). The same dose of roentgen irradiation may produce tanning on one person and depigmentation on another (Wachtel). In several cases personally observed by one of us, an x-ray dose of from one eighth to one fourth unit, barely one eighth of that sufficient to cause a slight erythema on the average person, brought out within seventy-two hours a crop of black moles hitherto unsuspected by either physician or patient. Ultraviolet irradiation just adequate to stimulate repigmentation of vitiligo plaques, will, if increased ever so little beyond the optimum for a given person, result in a sudden disappearance of the newly formed pigment (Hashimoto). Among solar leukodermas, in Tommasi's paradoxical case, parts of the body exposed to the sun were uniformly depigmented, while parts protected by the bathing suit were slightly and uniformly hyperpigmented, giving a bathing-suit design exactly the reverse of that usually observed. Kyrle (reference 29*a*) was convinced that a congenital inferiority of certain circumscribed skin areas was the deciding factor in many cases of vitiligo. Such areas may not be suspected until some combination of other factors makes unusual demands on the skin functions. Circumscribed areas deficient in normal pigment have been shown to exist in the skin of patients with psoriasis, on parts not yet invaded by the eruption (Van Kerckhoff). In these cases, there is evidently a deficiency in the keratinization function, as well as in melanogenesis. In

the cases of true vitiligo associated with retention of arsenic, however, only the pigment function appears (or remains) impaired. This does not mean that the disturbance is limited to the skin, nor that arsenic is necessarily the sole factor. As in a severe exfoliative dermatitis the entire system is involved, so it seems probable that a relative or potential deficiency of certain skin areas or functions constitutes only one of several weak links in the vital chain of the so-called "susceptible" person. A sluggish excretory mechanism may constitute another weak link. Arsenic may be only the exciting force, or, as we prefer to say, pending further proof, one exciting force.

It has been shown repeatedly that the size of the dose is of little significance compared to the factor of individual variation. Cases of melanosis have been reported as occurring after as little as 0.26 Gm. of arsenic acid (Waelsch, cited by Stahl) and 0.3 Gm. of the same drug (Müller, cited by Stahl). No parallelism could be detected in our own cases between the amount of arsphenamine received by a patient and the extent, nature or intensity of his or her pigmentary changes. In an effort to obtain further light on the problem of individual (or group?) susceptibility to arsenic, we carried out on our patients with vitiligo intradermal tests with arsphenamines in various dilutions. Since these tests form part of a more extensive series, to be reported separately, we shall confine ourselves here to a brief presentation of the facts. Findings for each case are summarized under the individual case reports.

We considered a reaction positive (+) when a papule or nodule from 3 to 15 mm. in diameter formed on the site of the injection. The papule or nodule might appear within a few days after the injection, or not until one, two or three weeks later. It might begin as a pinhead-sized elevation and only gradually increase in size. In some instances an area of dermatitis developed around the nodule (+ D). These positive reactions usually involuted slowly, sometimes persisting for several months. When a cyanotic or an infiltrated spot developed at the site of injection, we considered the reaction as doubtful (±), even when it persisted for several weeks or a month. These less pronounced reactions, however, usually subsided within one or two weeks. A transitory macule, which disappeared within the first few days, was considered negative. A solution of potassium arsenite and water, used intradermally as a control, never gave positive reactions. By referring to the tables in the various case reports, one may follow the patients' responses to the injections. It is interesting to note that the fourth patient (T. L.), who had the highest amount of arsenic in the skin (5.22 mg.) and also high percentages in the blood and urine, gave a most pronounced reaction to the intradermal tests, showing a dermatitis around the sites of injection with both neoarsphenamine and old arsphenamine.

Numerous writers have sought to explain vitiligo as a consequence of injury or functional disturbance of the nervous system. Recently, Dohi and Korhonen have taken the view that loss of skin pigment might be brought about by injury to the sympathetic nervous system through the toxic action of arsphenamine. These writers base their arguments chiefly on (1) function tests of the sympathetic nervous system carried out on their respective patients with vitiligo (one each), following arsphenamine dermatitis, and (2) the well-known occurrence of the "angioneurotic complex" or nitritoid crisis and similar though milder reactions following immediately on the intravenous injection of arsphenamine.

The cause and mechanism of these immediate reactions are still much debated. If they have a common origin with the more delayed cutaneous reactions—dermatitis and pigmentary changes—we should expect to find, among patients giving immediate vasomotor reactions to the injection of an arsphenamine, a higher incidence of the skin manifestations; and conversely, in the histories of patients with dermatitis, melanoderma and vitiligo, we should expect some previous indications of neurocirculatory instability, in the form of nitritoid crises or one of the milder forms of vasomotor reaction to earlier injections of the drug. We have not observed any such concurrence, either in the cases under discussion here or in a series of cases of arsphenamine dermatitis studied previously from the standpoint of various complications (Cannon and Karelitz), and we are not aware that it has been reported in significant numbers by others. Kyrle considered the two reactions to be based on different processes. In his experience, patients with a tendency to the "angio-neurotic complex" were as a rule not subject to dermatitis, while those highly susceptible to dermatitis did not customarily react with angioneurotic complications, but would tolerate a number of injections without any apparent difficulty, before the onset of the dermatitis. The Salvarsan Committee of the British Medical Research Council, after its study of extensive series of cases from both groups of complications, concluded that exfoliative dermatitis and inflammation of internal organs as well were attributable to the arsenic per se, the findings corresponding to those in acute poisoning from inorganic arsenic; whereas, the "vasomotor" phenomena, including the nitritoid crisis, pointed to a disturbance of the colloidal condition of the blood not directly connected with the presence of arsenic in the arsphenamine molecule. Without presuming to have made a comprehensive review of this phase of the subject, we do not feel that evidence so far available warrants placing two such diverse phenomena on a common basis.

The functional tests of the vegetative nervous system carried out by Dohi and by Korhonen appear to have yielded but two responses indicative of any peculiarities in their patients: dermographism and

sweating. Both writers obtained a more pronounced urticaria factitia alba on the depigmented areas than on the hyperpigmented ones (normal areas on Dohi's patient negative). After injection of pilocarpine, both found sweating absent or nearly so on the depigmented areas, though increased elsewhere. Epinephrine also produced slight glycosuria in Dohi's patient (Korhonen's negative), though the more recent experiments tend to minimize the significance of minor amounts and variations of urinary sugar.

In view of the scarcity of published reports on this phase of the subject, and the none too conclusive nature of those which have come to our attention, we thought it well to investigate in our own group of patients the possibility that arsenic retention might have led to loss of pigment by way of injury or functional derangement of the sympathetic nervous system. At least, symptoms of any such disturbances occurring uniformly in a number of cases with the vitiligo-arsenic factors in common, might be considered significant. Before carrying out our tests, we had three of the four patients examined in the endocrine department. The condition in one (case 2) was diagnosed as possible hypothyroidism with goiter; the other two patients (cases 1 and 7) revealed nothing suggestive of endocrine disturbances. Details of the nervous system tests and responses may be seen in table 2.

Of the four patients tested, I. T. (case 2) was the only one whose reactions as a whole were indicative of any functional imbalance. Here, the fall in blood pressure after epinephrine, together with the somewhat exaggerated response to pilocarpine (excessive salivation, vomiting and state of anxiety) might well be construed as symptoms of abnormal vagus tone. The increase in pulse rate after the administration of pilocarpine is also somewhat higher than usual. Lehmann (cited by Müller) found that persons with an increase of from fifteen to twenty beats after subcutaneous injection also showed other symptoms of hyperexcitability of the vagus. The reactions of the remaining three patients to the pharmacodynamic tests were with few exceptions within the limits generally found in normal persons, and the divergences were too lacking in uniformity to enable any conclusions to be drawn, without a more careful inquiry into other factors. The tests for dermographism, the Loewi phenomenon and the pilomotor reflex were uniformly negative in all four patients, and Aschner's phenomenon was within the limits observed in healthy subjects.

The most interesting observation, in our opinion, was the sweating response to pilocarpine. Patients in cases 1 and 7 showed sweat droplets on normal parts but none on vitiliginous parts. This is in conformity with the findings of Dohi, Kerhonen and other investigators. In the second patient, however, sweat droplets appeared on both normal and vitiliginous parts, but none on the shoeblack spots. It is quite possible that some connection exists between these local abnormalities of both

TABLE 2.—*Functional Tests of Vegetative Nervous System in Patients with Vitiligo*

Case	Drug*	Pulse	Blood Pressure	Glycosuria	Pupils	Saliva	Sweating	General	Aschner's Phenomenon	Loewi Test	Dermographism	Pilomotor Reflex
1. D. R.	Epinephrine	+2 −4 +2	Unchanged	Negative	.....	.....	.....	.....	−8 (68-60)	Negative	Negative	Negative
	Pilocarpine	+20	+ 4	.....	.....	50 cc. in 1 hour	Sweating over face, chest, scalp; none over back and extremities; none on vitiliginous areas					
	Atropine	−12	−10 (120/94)	.....	Unchanged (5 mm.)							
2. I. T.	Epinephrine	+ 4	−20	Negative	.....	.....	.....	.....	Unchanged (80-80)	Negative	Negative	Negative
	Pilocarpine	+24	+38	.....	.....	130 cc. in 1 hour	Sweat droplets appeared on normal skin and vitiligo; none on shoe-black spots	Vomiting, state of anxiety; symptoms resembling mild angina pectoris; pressure in region of heart				
	Atropine	− 8	−4 mm. Hg (120/80)	.....	+ 2 (5 to 7 mm.)							
3. S. R.	Epinephrine	+ 8	+ 6	Negative	.....	.....	.....	.....	−10 (86-76)	Negative	Negative	Negative
	Pilocarpine	+ 8	−10	.....	.....	220 cc. in 40 min.	Skin became slightly moist	State of anxiety; urinary urgency; pressure in epigastrium				
	Atropine	− 8	−15 (104/90)	.....	+ 2 (4 to 6 mm.)							
7. C. J.	Epinephrine	−20	+56	Negative	.....	.....	.....	.....	−10 (80-70)	Negative	Negative	Negative
	Pilocarpine	+20	+15	.....	.....	95 cc. in 1 hour	Sweat droplets present on normally pigmented parts; absent on vitiliginous parts					
	Atropine	−4 −10 in 40 min.	Unchanged +4 in ½ hr. (120/90)	.....	+ 3 (5 to 8 mm.)							

* Epinephrine, 0.001 Gm. subcutaneously; pilocarpine hydrochloride, 0.01 Gm. subcutaneously; atropine sulphate, 0.001 Gm. subcutaneously.

sweating and pigmentary functions, and a disturbed equilibrium of the vegetative nervous system. Dohi's case was diagnosed as "sympathicotonic;" our case 2 might be called "vagotonic" by the same criteria. But it is well to remember that the diaphoretic action of pilocarpine has not yet been satisfactorily explained. Many other effects of the drug parallel those obtained by physiologic stimulation of the parasympathetic nerves, yet so far, only sympathetic innervation has been demonstrated for the sweat glands.* In the face of even greater uncertainty concerning vegetative control of the pigment function, conclusions would obviously be premature.

To sum up our findings for functional tests of the vegetative nervous system: Four patients with vitiligo were tested, three with a history of arsphenamine dermatitis and one with evidence of arsenic retention but without dermatitis or any history of arsenical medication. Of these four patients, three (including the one without dermatitis) gave responses with only occasional minor variations from those commonly obtained from normal persons. A fourth gave some responses which might be construed as "vagotonic," while others (dermographism, Aschner and Loewi phenomena, pilomotor reflex) were negative. In view of these facts, we do not feel that we could prove, even with a greater series of cases, any definite relation between the development of vitiligo and the vegetative nervous system. One must also make allowance for the many divergences of opinion, even among specialists in this field, as to what constitutes normal and abnormal responses to the various tests; and the tests themselves, granting the necessity of some more or less arbitrary standards of interpretation, can give at best only a very fragmentary picture of the workings of a mechanism as complicated as that of the human nervous system. In weighing the results of our experiments, we have merely followed the criteria set forth by critics such as Kuntz, Sollmann, and Müller and his collaborators.

CONCLUSION

We incline to consider the retention of arsenic in the system, evidenced by positive findings in the blood, urine and skin, as the exciting factor in the development of vitiligo in our cases. The simplest explanation would be that the arsenic or its metabolites act directly on the vital cells of the epidermis, of which the basal layer is known to be the site (and possibly the only one) of cutaneous pigment formation in man. Sometimes depigmentation proceeds without other visible signs of injury. Under other conditions (more rapid oxidation? lower

* Dieden, on the basis of animal experiments reported in 1915, claimed to have produced evidence of parasympathetic fibers of inhibitory nature, but these findings have not been confirmed by subsequent investigators, according to Kuntz (reference 28).

individual tolerance?) these more subtle changes are masked in their initial stages by inflammatory processes as already described.

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PUSTULAR PSORIASIS

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The pustular form of psoriasis is rare in North America. Since the publication of papers by Barber [1] and Ingram [2] in 1930, numerous cases have been seen and recognized in England. The discussion on the most recent case presented by Barber [3] shows that many dermatologists are not convinced that the palmar and plantar eruptions described are psoriatic. The only reference found in the American literature to the pustular form of psoriasis is by McCarthy,[4] who states: "The collection of leucocytes in the epithelium is always in proportion to the intensity of the process and in some cases is so extensive as to warrant the name, psoriasis pustulosum." However, McCarthy does not elaborate further on this phase of psoriasis and makes no mention of pustular palmar and plantar lesions. The following case is reported as pustular psoriasis of the palms and soles associated with psoriasis vulgaris on the usual sites.

History.—A Canadian girl, aged 15, of English parentage, had had no skin eruption previous to November, 1932, when she first noticed patches of thick, dry scales on her scalp. Then, within a few days, the thenar eminences of both palms became simultaneously involved in a reddish, slightly scaling eruption. A few days later, the inner side of the left instep, followed in a day or two by the right, became affected. Then the patient noticed discrete, reddish scaling areas on the front and back of the chest and on the extensors of the arms and forearms. Two months later, similar lesions appeared on the extensor surfaces of the legs, and a month after this the right thumb and fifth fingernails were seen to be dot-pitted. The patient had always been well, apart from periodic attacks of tonsillitis. She had had no sore throat immediately preceding the onset of the cutaneous eruption.

Examination.—The patient reported at the clinic on Dec. 18, 1932, about two weeks after the onset of the scaling on her scalp. She appeared to be well developed and well nourished. The general medical examination of the patient

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From the Department of Medicine, University of Toronto and Toronto General Hospital.

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revealed nothing abnormal. The examination of her throat revealed moderate-sized, cryptic tonsils which were not inflamed. The mucous membranes appeared normal. The examination of the skin showed thick, dry scales on the scalp and discrete, salmon red areas on the extensors of the arms and forearms and on the back and front of the trunk. These areas varied from 0.5 to 1.5 cm. in diameter and were covered with a dry micaceous scale. When this scale was removed, the typical bleeding points of psoriasis could be seen. Involving the thenar eminences of both palms (fig. 1), the inner surface of the left and, to a less extent, of the right instep, were reddish, scaly areas. The scaling on the soles was much thicker than that on the palms (fig. 2). On closer examination, minute brownish crusts and minute white pustules, neither of which were larger than the head of a common pin, were seen distributed throughout these areas. The lesions were more numerous on the palms than on the soles. Both pustules and crusts were very superficial. When the former were opened with the point

Fig. 1.—Palmar lesions; the tiny crusts are just visible in the center of the right palm. The pustules cannot be seen in the photograph. The biopsy section was removed from the left thenar eminence.

of a scalpel, the amount of fluid which they contained was seen to be minute. These pustules and crusts are the characteristic features of pustular psoriasis.

Laboratory Examination.—(*a*) Serological: The Wassermann and the Kahn reactions were both negative. (*b*) Bacteriologic: Repeated cultures of the intradermic pustules on the palms and soles were made in a tryptic digest broth and on Sabouraud's proof medium, and all but one, which grew Staphylococcus albus, were completely sterile. No fungus was found on repeated direct examination of the scales and pustules mounted in 20 per cent potassium hydroxide. Histopathologic: A small elliptic piece of skin was removed from the left thenar eminence. The tissue was embedded in paraffin; serial sections were cut, 6 microns in thickness, and stained with Harris' hematoxylin and eosin. The following is the histopathologic report:

"Microscopically, marked inflammatory changes were seen in both epidermis and corium. In the former, there was slight thickening of the stratum corneum

with imperfect cornification. This was shown by the presence of nucleated cells on the surface and by the formation of scales containing serum and leukocytes. A study of serial sections revealed the presence of several small collections of leukocytes lying in the upper rete or in the stratum corneum (fig. 3). Under higher power magnification, these leukocytes were seen to be chiefly polymorphonuclears together with a few lymphocytes. As these collections of leukocytes showed central liquefaction, they might be considered as true miliary, epidermal abscesses

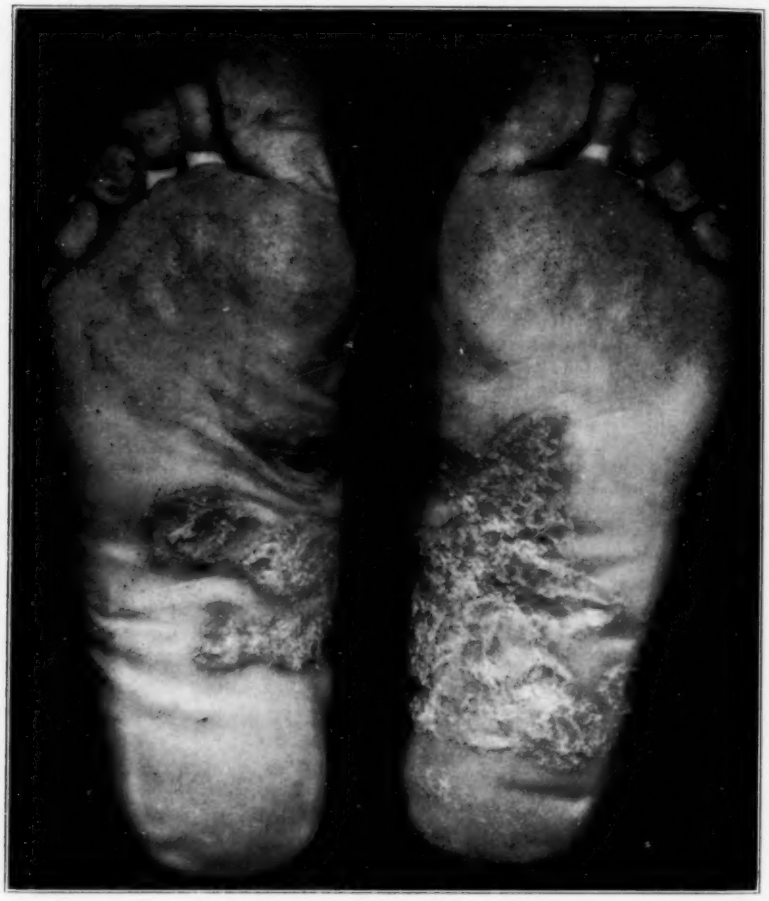

Fig. 2.—Plantar lesions, showing scales more abundant than on the palms. The crusts are just visible on the left sole. The skin on and about the toes was quite clear; the dark spots shown were particles of dirt.

(fig. 4). (They correspond to the pseudo-abscesses of Munro-Sabouraud seen in psoriasis vulgaris. They are larger, however, in fact sufficiently large to be seen macroscopically as the pinhead-sized pustules previously described). The stratum granulosum was increased in some regions and absent in others (fig. 3). The stratum mucosum showed a fairly regular thickening, and the interpapillary pegs were long and broad. The rete cells surrounding the miliary abscesses were

swollen and separated by small amounts of serum. A migration of polymorphonuclear leukocytes was seen proceeding from the papillae toward the abscesses (fig. 4).

"In the corium, the most marked changes consisted of a dilatation of the papillary blood vessels and an infiltration of lymphocytes about them (fig. 3). The papillae were long, narrow and slightly clubbed at their outer extremities, and were covered by only one or two layers of rete cells in many places. They were edematous, particularly the ones which lay under the abscesses. The reticular portion of the corium showed some dilatation of the blood vessels, slight edema and a perivascular infiltration of leukocytes, most of which were of the lymphocytic type."

Differential Diagnosis.—The other probable diagnoses of the palmar and plantar lesions besides pustular psoriasis are:

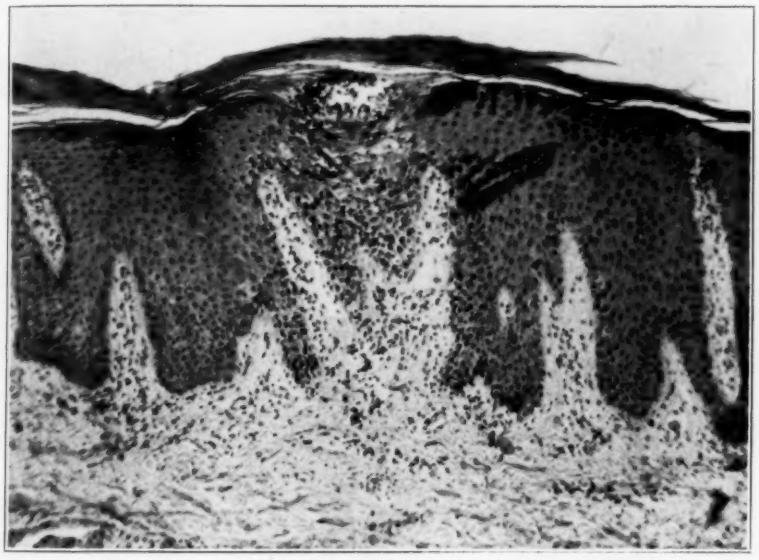

Fig. 3.—Pustular psoriasis; parakeratosis; micro-abscess; acanthosis; leukocytic infiltration beneath the micro-abscess; dilatation of papillary blood vessels (× 100).

(*a*) Acrodermatitis continua or dermatitis repens (Crocker). Barber [1] and Ingram [2] have stressed the differentiation between this condition and pustular psoriasis. The chief points eliminating acrodermatitis continua are: lack of history of injury, symmetry of the eruption, simultaneous appearance of lesions on the palms, presence of psoriasis vulgaris elsewhere, sterile culture of the pustules and the histologic picture which possesses the cardinal histopathologic features stressed by Montgomery.[5]

(*b*) Dermatomycosis. Fungus infection is ruled out on the previously stated points and on the fact that fungus could not be demonstrated on repeated direct examination.

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(*c*) Epidermophytosis, trichophytosis and moniliasis. Secondary toxic eruptions are ruled out on account of the absence of any primary mycotic lesions.

(*d*) Infectious eczematoid dermatitis. The history of onset, the absence of furuncles previous to the eruption, the macroscopic appearance and the sterile cultures of the pustules make the diagnosis of this condition appear to be extremely unlikely.

(*e*) Syphilis, occupational dermatitis and eczema. Andrews[6] states: "The palms and soles are rarely affected. Most cases so diagnosed eventually are proved to be due to syphilis, occupational irritants or eczema. Psoriasis does, however, at times affect these areas, forming diffuse erythematous, dry, scaling

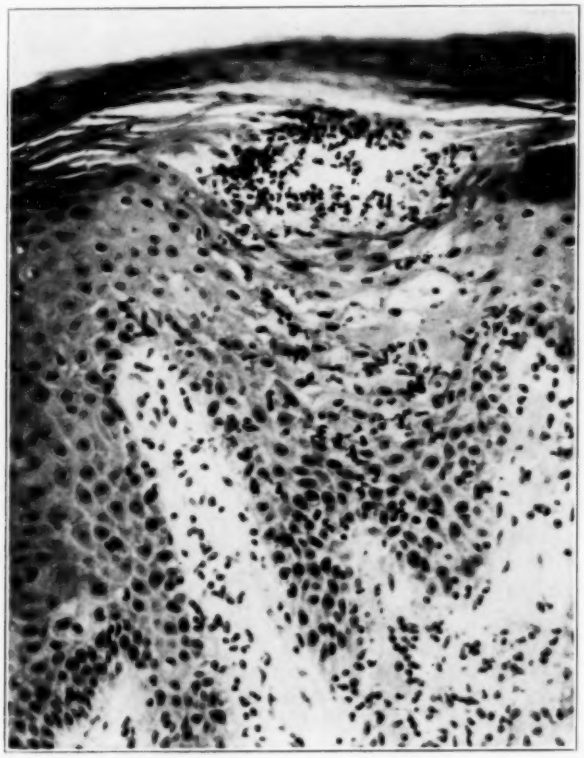

Fig. 4.—Higher power magnification of figure 3. Abscess formed chiefly of polymorphonuclear leukocytes; edema and leukocytic infiltration of rete deep to micro-abscess; lymphocytic infiltration of papillae (× 200).

patches, or circumscribed, verrucous thickenings, sometimes linear." The absence of other syphilitic signs, the negative Wassermann and Kahn reactions of the blood, and the histopathologic picture make a diagnosis of syphilis untenable. As far as could be learned, the patient handles nothing at school or at home which might be the cause of a dermatitis venenata. The condition is not eczema of the palms and soles. The history, clinical appearance, histopathologic picture, and the presence of psoriasis elsewhere confirm this statement.

6. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930, p. 435.

COMMENT

According to Barber [1] and Ingram,[2] Strandberg was the first to suggest the possibility of these palmar lesions being psoriatic. Ingram states that Macleod was one of the first to suggest the term "pustular psoriasis." It is a very appropriate title; it describes the macroscopic and microscopic appearances of the lesion well and has the added virtue of being a simple English term.

Barber [3] recently stressed the importance of tonsillar infection in the causation and the removal of this focus of infection as an aid to treatment of the condition. He cites three cases in which removal of the tonsils caused either complete recovery or converted the pustular form of psoriasis into the common type. The patient whose case is recorded here gave a history of repeated attacks of tonsillitis, and tonsillectomy has been advocated. That these cases are notoriously difficult to clear up is mentioned by several who took part in the discussion.[3] Goeckerman's [7] method of using crude coal tar and ultraviolet light would be well worth a trial in view of his success in treating psoriasis vulgaris and erythroderma psoriaticum.

There are many arguments against the contention that these palmar and plantar lesions are psoriatic. However, it must be admitted that, bearing the following facts in mind, it is difficult to dismiss the diagnosis of pustular psoriasis: (*a*) history of a scaly eruption on the scalp followed in a few days by the simultaneous appearance of pustular lesions on the palms and then on the soles; after that, the appearance of typical psoriatic lesions on the trunk, arms and legs and finally dot-pitting of the finger-nails; (*b*) negative results in the search for fungi and bacteria in the pustules and scales; (*c*) a histopathologic picture which embraces the features of psoriasis vulgaris except that the micro-abscesses have enlarged sufficiently to be visible to the naked eye.

SUMMARY

1. A case of pustular psoriasis of the palms and soles, associated with psoriatic lesions on the usual sites, is recorded.

2. The laboratory observations confirm the clinical diagnosis.

3. The name "pustular psoriasis" is ideal for this form of psoriasis.

NOTE.—Ebert's [8] excellent paper on "A Psoriasiform Eruption with Pustular Exacerbations" appeared after the writing of this article. It is felt that the present article will supplement his findings and add proof to the contention that a pustular form of psoriasis does occur, although, admittedly, infrequently.

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7. Goeckerman, W. H.: Treatment of Psoriasis, Arch. Dermat. & Syph. **24**:446 (Sept.) 1931.

8. Ebert, M. H.: A Psoriasiform Eruption with Pustular Exacerbations, Arch. Dermat. & Syph. **27**:933 (June) 1933.

NICKEL ECZEMA

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CINCINNATI

Ever since Blaschko [1] first described the dermatitis associated with galvanizing, this condition has played a practical rôle in dermatology. Schittenhelm and Stockinger [2] wrote that nearly every one who does this sort of work sooner or later becomes eczematous. If this is true, the condition has not only a practical importance but also an interesting theoretical aspect. Its frequent occurrence would show that nickel is one of the rare substances to which every one can be sensitized. In support of this theory, Walthard [3] demonstrated that he was able to sensitize guinea-pigs regularly with nickel.

This whole theory of nickel as a uniformly sensitizing substance, however, does not hold true. The experiments of Walthard [3] have not been confirmed by other workers. In the investigations of Schittenhelm and Stockinger,[2] it is peculiar that positive reactions to the nickel test were obtained only on areas of skin previously affected. It is true that such localized sensitivity can be observed in eczema (J. Jadassohn, Stauffer [4]), but generally this is not the case. In most patients—those with primrose eczema, for example—the whole skin becomes sensitized. Moreover, other investigators [5] who have made similar studies of nickel eczema have found it not nearly so frequent in galvanizers as was suggested by Schittenhelm and Stockinger.[2] In a recent article on nickel dermatitis, Dubois [6] said that there are two types of nickel-plating factories. In one, huge electrodes are made; here the workers dip their arms into baths containing 35 per cent nickel sulphate, 18 per cent magnesium sulphate and from 0.1 to 0.2 per cent sulphuric acid and

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From the Dermatologische Klinik, University of Zürich.

1. Blaschko, A.: Die Berufsdermatose der Arbeiter. Ein Beitrag zur Gewerbehygiene. I. Das Galvaniseur-Ekzem, Deutsche med. Wchnschr. **15**:925, 1889.

2. Schittenhelm, A., and Stockinger, W.: Ueber die Idiosynkrasie gegen Nickel („Nickelkrätze") und ihre Beziehung zur Anaphylaxie, Ztschr. f. d. ges. exper. Med. **45**:58, 1925.

3. Walthard, B.: Die Erzeugung experimenteller Nickelidiosynkrasie bei Laboratoriumstieren, Schweiz. med. Wchnschr. **24**:603, 1926.

4. Stauffer, H.: Die Ekzemproben, Methodik und Ergebnisse, Arch. f. Dermat. u. Syph. **162**:517, 1931.

5. Jadassohn, W., and Schaaf, F.: Ueber die Haüfigkeit des Vorkommens Nickelekzemen, Arch. f. Dermat. u. Syph. **157**:572, 1929.

6. Dubois, C.: La dermite du nickel, Schweiz. med. Wchnschr. **1**:278 (March 21) 1931.

maintained at a temperature of 85 C. The air of the workrooms is filled with the thick vapors from these baths. Among 370 persons employed at this type of work, Dubois found only 20 who were able to continue without interruption for two years (1928 to 1929). The hands were affected primarily, and the condition was more marked in those areas where the clothes, impregnated with these vapors, rubbed the skin. Dubois [6] associated these findings with those of Schittenhelm and Stockinger,[2] and he added that similar observations had been made in a large factory in Oslo. On the other hand, Dubois [6] confirmed the assertions of W. Jadassohn and Schaaf,[5] since he found that among the workers in smaller, ordinary shops nickel eczema was rather exceptional. These observations are of great practical importance because of the high percentage of cutaneous inflammations seen in the large factory. Furthermore, Dubois [6] has not proved, and it does not seem even probable, that nickel was the causative agent of the cutaneous disease which he described. So long as tests with nickel salts, magnesium sulphate and sulphuric acid—all substances used in the baths—were not made, nickel cannot be considered the sensitizing agent. In view of the special conditions under which the people worked, the omission of skin tests and the rarity of cases in the smaller shops, one cannot quite understand how Dubois claimed to have upset the statistical contributions of W. Jadassohn and Schaaf.[5] Nickel is not the only possible sensitizing substance which could play a part in the development of this condition. Lime can cause eczema. W. Jadassohn and Schaaf [5] wrote of an eczema in a nickel-worker in whom only the tests with lime were positive and who later was able to continue his work as a nickel-plater after the particular type of lime used was changed. As a prophylactic measure, Sallenbach [7] studied 2 women applicants for nickel-plating. They had no cutaneous changes, and tests with nickel were negative, but 1 woman reacted strongly to the lime which she was to use. If she had been allowed to work with this lime, eczema would probably have developed, and without tests, this would have been considered nickel eczema.

Thus it seems necessary to have a larger number of well observed cases, particularly because nickel is one of the most widely used metals. It is probable that it can be the causative factor of eczema, even when it is not suspected. Lain [8] reported a dermatitis from the use of eyeglasses, and he believed, but did not prove, that nickel was the cause of this condition. Dubois [9] recently described a case of eczema which occurred

7. Sallenbach, Lilly: Zur Prophylaxe des Gewerbeekzems, Arch. f. Gewerbepath. u. Gewerbehyg. **1**:793, 1931.

8. Lain, E. S.: Nickel Dermatitis: A New Source, J. A. M. A. **96**:771 (March 7) 1931; Zentralbl. f. Haut- u. Geschlechtskr. **38**:75, 1931.

9. Dubois, C.: Contribution à la dermite des parures, Ann. de dermat. et syph. **3**:209 (March) 1932.

from the wearing of nickel-plated wrist-watches, and in each of these cases he was able to demonstrate a cutaneous reaction to pieces of money which were almost pure nickel. If any definite conclusions are to be made, one condition—mention of which has been missing in the different publications—must be fulfilled, namely, that by means of the nickel test it must be shown that it is nickel and not some other substance which is causing the eczema. Schittenhelm and Stockinger [2] made tests, but these were positive, as mentioned before, only on areas previously affected. Intracutaneous and subcutaneous injections were also made by these investigators, and focal reactions were noted. In a case on record at the Swiss Industrial Insurance Office (W. Jadassohn and Schaaf [5]), the nickel tests were positive even on skin not previously involved. Stauffer [4] reported two cases of nickel eczema with positive reactions to the nickel test on the intact skin. Among the other early proved cases of nickel eczema were those of Gerstein,[10] Fuhs,[11] Lewith [12] and Feit.[13] Steiner [14] claimed that a large percentage of persons with neurodermatitis, more than 50 per cent, show positive reactions to the nickel test.

It seems clear that real progress in the whole subject of allergic eczema can be made only by following exactly the method of testing indicated by J. Jadassohn and Bloch. First, the skin of the patient must be tested, that is, with a patch test. This test, made with the substance claimed to be the cause of the given eczema, must give a clearly positive reaction on skin not previously affected; the test must be made with a concentration which is harmless for normal skin. Generally, this patch test must be positive on uninvolved skin, but there are exceptions to this rule in the rare cases of sensitivity localized to previously pathologically changed skin. The second condition necessary is that when the questionable substance is wholly removed for a long time from any contact with the skin, the eruption must show a tendency to spontaneous healing.

It is evident that it is much more difficult to fulfil these requirements in those cases in which there is not a mono-idiosyncrasy but a poly-idiosyncrasy, and also in those cases in which the idiosyncrasinogen is transported hematogenously into the skin, and small traces probably remain in the tissues. At any rate, one cannot assume that a substance

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10. Gerstein: Verhandl. d. Essen dermat. Gesellsch., January, 1927; Zentralbl. f. Haut- u. Geschlechtskr. **23**:163, 1927.

11. Fuhs: Zentralbl. f. Haut- u. Geschlechtskr. **24**:750, 1927.

12. Lewith, R.: Zentralbl. f. Haut- u. Geschlechtskr. **26**:348, 1928.

13. Feit: Dermatitis Venenata (Nickel-Plating Solution), Arch. Dermat. & Syph. **21**:481 (March) 1930.

14. Steiner, Karl: Ueber die Ergebnisse und den Wert der „funktionellen Hautprüfung" mittels der Läppchenprobe bei Hautkranken und bei Haut-„Gesunden," Arch. f. Dermat. u. Syph. **157**:600, 1929.

used in the working process is the main or only factor in the development of subsequent cases of dermatitis until it has been shown that these patients are specifically sensitive to this substance, and that no other materials concerned in the process play a rôle. This requirement is especially important, because no industrial process exists in which not several but many potential idiosyncratic substances are employed. Moreover, in the galvanizing process, if the skin is injured by any caustic material and the superficial layers of the skin, the epidermis, are removed, nickel produces inflammation regularly on this denuded skin, but this inflammation is not an eczema.

REPORT OF CASES

Case 1.—E. W., aged 19, a nickel-worker, was admitted to the clinic on June 6, 1929. In the middle of May, 1929, he first began to work in a nickel-plating shop. After two days of work, an eruption appeared over the hands and arms, and in two weeks it had spread over the body. Pruritus developed for the first time only after several weeks. The patient was treated in the outpatient dispensary with tar suspension for a brief period without much improvement, and then was admitted to the hospital. He had never had a similar eruption. Previous to his employment in the nickel-plating shop, he had worked as a delivery boy. He had had rachitis, measles and a carbuncle in early childhood. In 1924, a severe generalized urticaria developed with a high fever; unfortunately, no additional details of this illness were known. In 1926, the patient was hospitalized for about five weeks for a suspected pulmonary tuberculosis. In 1927, he had a few small, desquamating areas on the back, breast, arms and lower extremities, supposed to be an infection from an animal (fungus?). The family history was without relevant details, especially as regards the allergic diseases.

General physical examination gave negative results, except for the changes in the skin. The eruption involved the entire body. On the face and trunk were numerous discrete, not follicular, reddish-blue papules the size of a pinpoint. Some of these had a small central vesicle. Many of the lesions were scratched, and long scratch marks were visible on the back and lower extremities. In some places these pinpoint-sized papules were confluent into ill-defined patches about 1 cm. wide. The skin of both antecubital fossae was infiltrated, rather markedly wrinkled, a bluish red, and covered with firmly attached white scales. Numerous small papules were found along the borders of these areas. Many scratch marks were also present on the extremities, and in some patches the denuded areas were 1 cm. across.

Patch tests were done with pure oil of turpentine, 5 per cent quinine, 5 per cent formaldehyde, a trace of arnica, iodoform gauze, primula, 5 per cent naphthalin spiritus and 0.1 per cent corrosive mercuric chloride. These tests were all negative, even after seventy-two hours. The following nickel tests were done, and the reaction measured according to the criteria of Bloch:[15] 1 per cent nickel sulphate, 3; 1 per cent nickel nitrate, 3; 1 per cent nickel chloride, 3 and nickel (metal), 0. Control tests with solutions of a nickel were negative on the normal skin of three persons. The patient also showed a reaction to soft soap, 1-2, in twenty-four hours, and 3-4 in forty-eight hours. Because lime has been shown definitely to have been the cause of some of these eczemas, a patch test with lime was done, with a

15. Bloch, cited in Stauffer.[4]

negative reaction. Because cobalt is so closely related chemically, a patch test with a 1 per cent solution of cobalt nitrate was done, but this was negative. The patient then exhibited a rather definite nickel idiosyncrasy.

After a brief period of secondary pyodermia, the eruption cleared up entirely, and the patient was discharged, four weeks after admission.

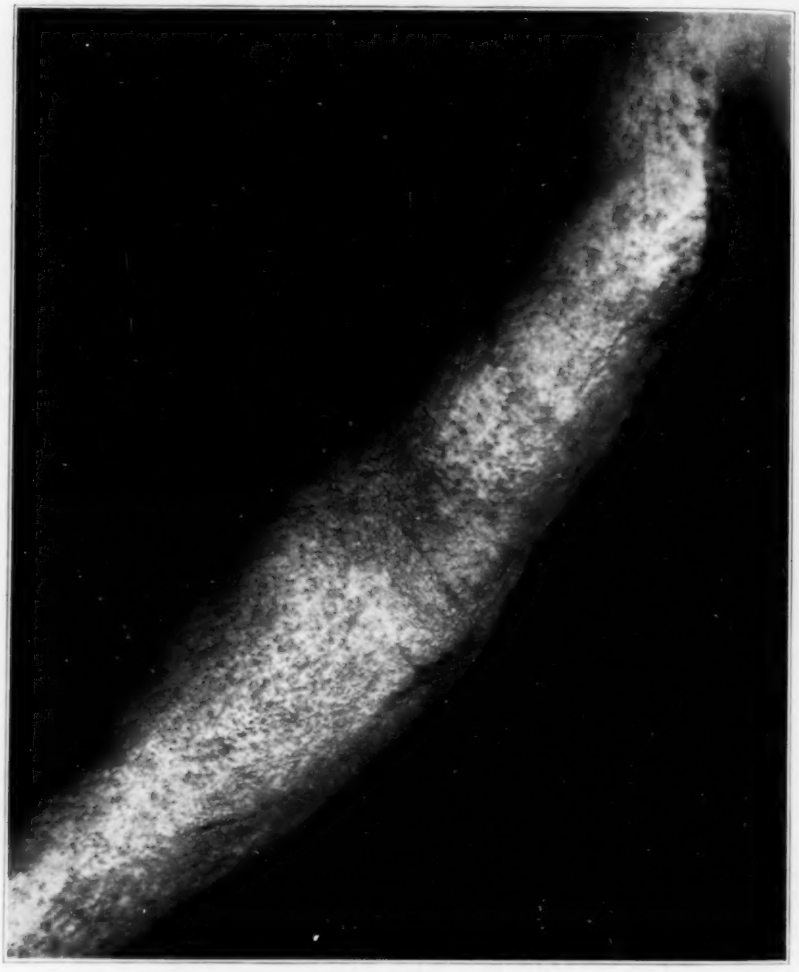

Fig. 1 (case 2).—Nickel eczema in a nickel-worker three days after beginning work.

Case 2.—G. D., aged 31 years, a nickel-worker, was admitted to the clinic on Jan. 6, 1933. After he had worked only three days in a small nickel-plating shop, working only with the bath, an acute dermatitis developed on the right hand, forearm, arm and face. Pruritus occurred immediately. The patient was accustomed to dip his right arm into the plating bath. He had never worked with nickel before. There was no history of any previous eruption of the skin or of asthma. He had

had attacks of hay fever for the past two years. The familial history was without relevant details. There had been no therapy prior to admission.

Except for the eruption, the physical examination gave negative results. The changes in the skin involved only the face and the entire right upper extremity. There was a diffuse redness of the face with many small papules scattered about. A diffuse and patchy erythema was found on the right hand, forearm and arm. This was more marked along the outer aspect. Along the inner aspect the erythematous areas were much smaller, and here especially there were numerous papules and vesicles varying in size from that of a pinpoint to that of a pinhead. The palmar surface of the hand was not involved. Many papules and small vesicles were found along the dorsum and sides of the fingers.

A patch test was done with Viennese lime (cold), and this remained negative, even after six days. Nickel tests were also done with the following reactions:

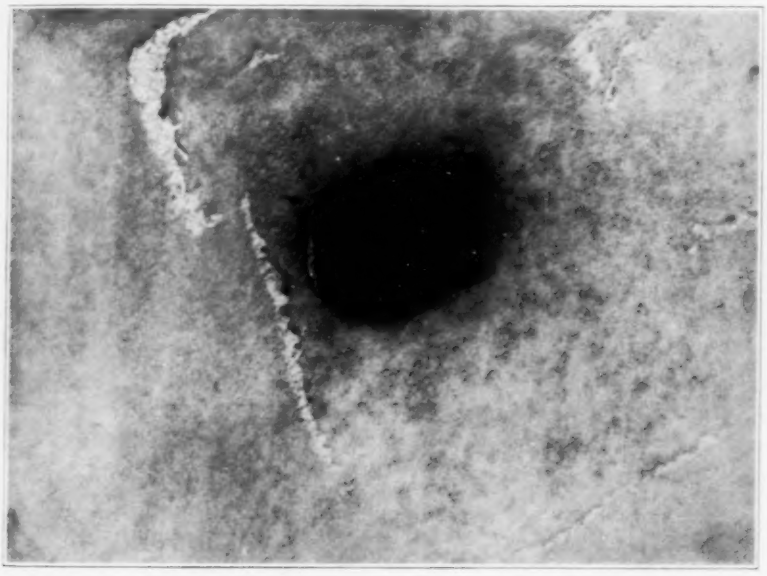

Fig. 2 (case 2).—Patch test with coin after twenty-four hours, showing a strong reaction with intense redness and numerous vesicles.

nickel sulphate (from the plating bath), 3; 10 per cent nickel sulphate, 3; 10 per cent nickel ammonium sulphate, 3; 10 per cent nickel propionic acid, 3; 10 per cent nickel aminopropionic acid, 3, and 1 per cent nickel lactate, 3.

This nickel-worker also showed a definite idiosyncrasy to nickel; he reacted positively to the nickel ion in the inorganic salts and in the organic salts. Cobalt tests were made with the following results: 1 per cent cobalt chloride, 0; 1 per cent cobalt ammonium cyanide, 0; 1 per cent pentaminocobalt chloride (aqueous), 0, and 1 per cent cobalt α-aminopropionic acid, 0. In this case also the cobalt tests were negative.

It is clear that in these cases the sensitivity of the skin is to the nickel ion in combination with either organic or inorganic acids. The specificity is so strict that the skin is negative even to the most closely related

chemical substance, cobalt. In the second case a test was made also with a complex nickel salt, 1 per cent sodium nickel cyanide. The reaction was as positive as with the simple salts. At first this seemed rather surprising because it is improbable that an organ like the skin, by simple contact, is able to change the complex salts into free nickel ions. However, the fact is not so peculiar, for the compound employed differs from the other inorganic complex salts, especially the cobalt salts, in a rather weak combination, and therefore nickel ions can be formed even by slight stimuli. This test, then, proved only the existence or presence of a high degree of sensitivity in the skin of the tested person, since only a slight concentration of nickel ions was sufficient to cause allergic manifestations.

Another point in the present analysis is that in both cases the cutaneous eruption manifested itself in so high a degree after so brief an exposure to the idiosyncratic agent. The commonest explanation for similar observations in the literature is that one is dealing with a congenital or even an inherited idiosyncrasy. Another means of explanation would be the assumption that the sensitization of the cell against a foreign substance can be developed rapidly in from twenty-four to forty-eight hours in exceptional cases. Generally this sensitization requires a certain longer time, from eight to ten days or more. In these special cases of nickel eczema still another explanation is afforded, namely, the gradual "silent" sensitization by nickel coins. Considering nickel coins and nickel-plated objects, nickel is a metal with which every one, from childhood on, comes in contact frequently. Moreover, this possibility should be thought of in cases of eczema of the hands, the cause of which otherwise cannot be explained. In the second case, a 20 centime Swiss coin, which is almost pure nickel, was used for a patch test, and twenty-four hours later a 3 plus reaction appeared.

Six weeks after discharge from the hospital, without resuming his work, the patient in case 2 had a recurrence. After a half day of pruritus, the eruption developed, at first with the same distribution as the original eruption, except that the right hand was not involved. The eruption remained localized for several days, and then became generalized. No lesions were present on the hands. Before the lesions became so widespread, patch tests with the 20 centime coin were made on the trunk, the palmar surface of the right hand and along the lateral aspect of the terminal phalanx of the middle finger of the right hand, proximal to the nail. Again the test on the trunk was strongly positive (3-4), but on the finger and palm no reaction occurred. Patch tests with 1 per cent nickel sulphate were made on the palmar surface of the left hand and on the thigh; on the hand the test was negative, and on the thigh, strongly positive. Tests with the coin and 1 per cent nickel

sulphate were negative on the soles. In addition, tests with bits of nickel-plated fastenings from the suspenders of the patient was strongly positive (3) on the upper part of the abdomen. Patch tests with pure turpentine, 3, 5 per cent formaldehyde and 1 per cent quinine (alcoholic) were all negative.

The patient had never had, so far as could be determined from the history, an eczema of the hands prior to admission to the hospital. Apparently a person can be sensitized to a substance without showing, at any time, appreciable clinical manifestations ("silent" sensitization). Bloch [15] observed this before with primin. This point of view is of practical as well as of theoretical importance. The fact that the patient did not show greater clinical signs previously can be explained by the special conditions under which the test was made. A twenty-four hour contact period was necessary, whereas for handling money, more frequent but briefer periods are required. There is another possibility, local desensitization from repeated contact, in spite of the negative patch tests on the soles. Of course, the marked thickness of the skin in these areas also should be considered as a factor in the production of clinically negative patch tests.

Of interest also is the fact that in both cases there existed an indication of previous allergic disturbances, urticaria in one and hay fever in the other. This is interesting because it is believed generally that in cases of purely exogenous idiosyncratic eczema the so-called allergic constitutional predisposition does not play an important rôle. It seems that this theory depends to a certain degree on the point of view of the investigator.

CONCLUSIONS

A review of current literature on nickel eczema is presented. The confusion between the various reports is explained by a lack of critical analysis of the cases, especially as regards the proof of the causative agent by means of the patch test. The cases of 2 nickel-workers with definitely proved nickel eczema are described. In each the eczema developed after only a brief period of contact, two days in one case and three days in the other case. These patients exhibited a remarkable idiosyncrasy to the nickel ion. Both gave negative reactions to cobalt solutions and to lime. The cobalt tests were done because of the close chemical relationship with nickel; the lime tests, because this substance has been shown to have been the cause of some of the cases of eczema in nickel-workers. Both of these patients had previous allergic disturbances, urticaria in one instance and hay fever in the other. One patient exhibited a strong reaction to a nickel coin. The practical value of nickel coins and nickel-plated objects as potential eczematogenic

agents is discussed. It is suggested that these be considered in the study of some of the eczemas of the hands with hitherto unknown etiology.

NOTE.—Since this paper was submitted, patch tests have been made on the uninvolved skin with 5 per cent nickel sulphate in 9 cases of neurodermatitis, and in no case did the test give positive results. In 3 cases patch tests were done with a nickel coin, and these tests likewise gave negative results. Stewart [16] recently reported, in great detail, a case of hypersensitivity to nickel. Tests also showed hypersensitivity to cobalt. As in the cases reported in this article, a background of many previous allergic disturbances was also disclosed in Stewart's case.

16. Stewart, S. G.: Inherent Sensitivity of the Skin to Nickel and Cobalt (Allied Elements in Group VIII, Periodic System), Arch. Int. Med. **51**:427 (March) 1933.

HEREDITARY CANITIES AND VITILIGO

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A group of pictures is submitted which seem to indicate without much doubt a distinctly hereditary tendency toward an absence of pigmentation in localized areas of the scalp and skin.

Fig. 1.—Photograph of the father, showing the absence of pigmentation in the hair and a suggestion of vitiligo on the forehead.

Figure 1, a photograph made several years before this report, shows the absence of pigmentation in the hair of the father and a suggestion of vitiligo on the forehead. Unfortunately no further photographic studies can be made of the father, because he is dead. The mother of the children stated, however, that he had vitiliginous areas on the body.

From the Pittsburgh Skin and Cancer Foundation.

Fig. 2.—Photograph of the elder daughter, aged 5.

3. Photograph of the younger daughter, aged 4, show-

Figure 2 shows D. E. W., aged 5, one of the children, and figure 3, M. J. W., aged 4, the other child. The location of the canities was the same in the father as in the daughters, and the vitiliginous areas on the bodies of the children correspond rather closely.

The hereditary tendency of this anomaly of pigmentation has frequently been noted in cases of vitiligo and of canities, but the clinical picture in the family group submitted is so striking that it was thought to be of interest.

631 Jenkins Building.

3. Photograph of the younger daughter, aged 4, show

Fig. 2.—Photograph of the elder daughter, aged 5.

A NEW CUTANEOUS MANIFESTATION IN THE SYNDROME OF VITAMIN A DEFICIENCY

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It may be presumptuous to refer to the dermatosis which I am to describe as "new." In these remote parts it is not easy to be sure whether an observation is original or not. I have searched such literature as is available, and have called in the assistance of both the librarian at Tavistock House, London, and Dr. Paul Unna of Hamburg, but no reference to the condition that I am describing has been found. If I am justified in my title I shall be the happier; if I am not, I can do no more than make my apology.

The general manifestations of vitamin A deficiency are now so well known that an account of them would be superfluous; the cutaneous changes, however, seem to be dismissed summarily with such references as "dryness of the skin," "acne" or "dermatitis with loss of fur" (in experimental animals). Pillat,[1] who is the only author to attempt a detailed clinical description, provided no histologic report. Even clinically, I should say that the cases which I shall describe and which I believe to show a pure cutaneous avitaminosis present a very different picture from those of Pillat. This point will be considered more fully later.

The discovery of this dermatosis was made at the quarterly inspection of the Uganda Central Prisons, during which every prisoner stripped in order that his skin might be examined. I was struck by the number of men, many of them of middle age, who presented the clinical picture of acne vulgaris combined with a dermatosis which none of the medical officers present could define. When Dr. H. B. Owen, who was examining the prisoners' eyes, segregated those suffering from night blindness and xerophthalmia, it was apparent that these men formed the bulk of those affected by the peculiar dermatosis. At subsequent monthly inspections of prisons, all new cases of this dermatosis were recorded, and it was found that the majority of these men suffered

Read at the Centenary Meeting of the British Medical Association in Nairobi. A short abstract is to be published in the East African Medical Journal.

1. Pillat, A.: Does Keratomalacia Exist in Adults? Arch. Ophth. **2**:256 (Sept.) 1929.

from night blindness and xerophthalmia, while almost every sufferer from xerophthalmia and night blindness showed these cutaneous changes. Up to the present, I have seen over 130 cases of this dermatosis.

CLINICAL DESCRIPTION

1. *Dryness of the Skin.*—This affects the whole body with the exception of the face and scalp. Both sebum and sweat seem to be deficient, except in the facial region, where they may be abundant. The normal lustrous skin of the native has, in these cases, become rough, dull and grayish black, the degree of grayness depending on the amount of desquamation present. These changes are most marked on the extensor surfaces of the arms, on the backs of the hands and front of the legs, on all surfaces of the thighs and across the buttocks.

Fig. 1.—Papular eruption on the outer side of the thigh.

2. *Itching.*—This is a prominent feature, and the dry parts usually show lines scored by the fingernails, which roughen the stratum corneum still further.

3. *Papular Eruption.*—This is typical of the condition, and has not been observed by me in patients not suffering from avitaminosis. The papules are about one-fourth inch (0.6 cm.) in diameter, smooth-topped, black and shiny. The edges are sharply demarcated, and the shape of these papules is round or polygonal. They are never as obtuse or coniform as the common acne papule. Their distribution is limited; almost invariably they are found on the extensor surfaces of the arms and on the front and outer surface of the thighs. In addition, they may be present to a variable extent on the buttocks, loins, chest and back. In the last two sites they frequently merge into the acneform eruption which is part of the syndrome.

4. *Folliculitis.*—In some cases there is an inflammatory swelling of the hair follicles, without the presence of pus. These inflamed follicles

usually present a broken hair projecting from the center, and may be an early stage of the papules already described.

5. *Acne.*—Here one cannot dogmatize. Many of the prisoners are young men who might be expected to present the picture of acne vulgaris outside the prison. Among the middle-aged, however, the presence of an acneform eruption must be of special significance, and the reaction of these persons to treatment indicates that this dermatosis, too, is a sign of vitamin A deficiency. Clinically, the papules differ in no way from those of acne vulgaris, except that pustulation is extremely rare—to my mind, a point of great interest. The distribution over the face, chest and back is also typical.

MICROPATHOLOGY

Papules were excised from 18 patients and examined microscopically. The histologic features of this condition are absolutely typical and never vary more than can be explained by the degree of severity of the condition.

The papule arises from a pilosebaceous follicle. Although this fact cannot be recognized on clinical examination, even with a lens, serial microtome sections invariably reveal a diseased follicle in the exact center of the papule.

The mouth of the follicle is completely sealed with a dense mass of horny tissue, the surface of which is flush with the horny layer of the surrounding skin. This follicular plug is composed of successive concentric layers of horny tissue, among which is seen a varying number of lymphocytes and polymorphonuclear leukocytes. The outer layers of this plug still show recognizable epidermal nuclei (parakeratosis) and are often in the form of a loose mesh. The plug occurs in the form of an inverted pear, the lowest part of which is superficial to the entrance of the sebaceous duct. In the substance of the plug one frequently sees the remains of the hair lying coiled up between the layers.

This appearance, of course, approximates to that of the common comedo, with important differences in distribution and the invariable absence of pustulation.

The skin adjacent to the follicle shows certain well marked changes:

Epidermis.—This becomes progressively thickened as one approaches the follicle, until at its margin, the stratum corneum has attained three times its previous thickness. As the stratum corneum of the remainder of the skin in these cases is definitely broadened, it will be seen that a considerable hyperkeratosis is a feature of the papules. The keratin tissue is loosely meshed, but no nuclei are seen; i. e., the parakeratosis is confined to the follicular plug.

The stratum lucidum and stratum granulosum are apparently normal in all parts.

The prickle cell layer undergoes marked acanthosis in the perifollicular region, and the interpapillary processes are markedly elongated. Individual cells are swollen and show active mitoses, while in the basal layer there are frequent distortion and reduplication of the cellular elements (an irritation phenomenon). Here, too, there is a degree of cellular infiltration with polymorphonuclear leukocytes varying with the severity of the case.

Corium.—This shows evidence of irritation; possibly the follicular plug acts as a foreign body and, with the additional irritation of the

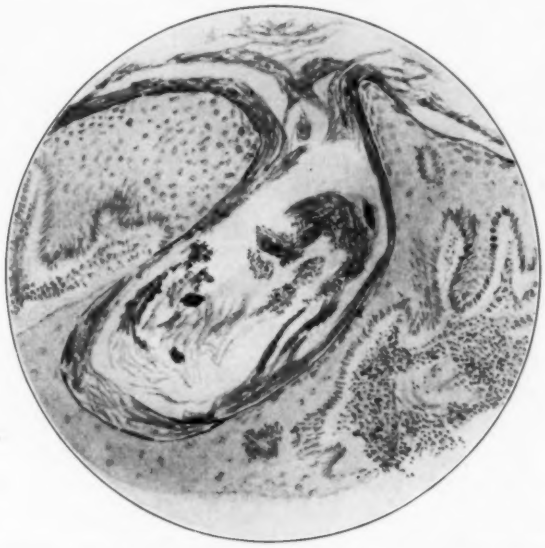

Fig. 2.—Photograph of colored drawing by the author. Hematoxylin and eosin stain; low power magnification.

surrounding acanthosis, produces a condition of perifolliculitis. There is a varying amount of congestion, edema and cellular infiltration, strictly limited to the neighborhood of the follicle; the cellular elements are chiefly lymphocytic and fibrotic, with a few endothelioid and polymorphonuclear cells. Eosinophils are rarely seen.

Apart from the separation of collagen bundles consequent on the edema and cellular infiltration, there is no alteration in the fibrous or elastic elements. Van Gieson's and Weigert's stains show a normal tissue structure.

During the active stage the amount of pigment per cell is slightly diminished in the basal layer of the epidermis, but, owing to the acantho-

sis and wrinkling of this layer, it is probably increased per square unit of surface, thus producing the striking blackness of the papule. The dermal chromatophores are not increased.

(These histologic changes are precisely the same as those of the papules of pityriasis rubra pilaris, though, of course, the two conditions cannot be confused clinically.)

The acne papule in this condition resembles that of acne vulgaris generally, with the exception that the cellular infiltrate is negligible; in one case observed it consisted merely of a dozen eosinophils in a section of the comedo. This, of course, tallies with the clinical observation that avitaminosis acne in my cases never led to suppuration.

During the process of cure, the papule shows the following changes: First, there is a spontaneous extrusion of its core, this process taking a week or more. At the end of this stage the papule has become less prominent and presents an open pit in the center. Later the pit shrinks and ultimately disappears completely, so that after from four to six weeks of treatment nothing remains except a marked black macule.

I have assumed this dermatosis to be the result of a dietary deficiency in vitamin A, and before embarking on an academic discussion must enumerate the points which led me to this conclusion.

The diet given in the Uganda Central Prisons at the time when these cases were found was as follows: maize, 20 ounces a day; beans, 5 ounces; meat (dry), 2 ounces; nuts, 3 ounces; salt, ½ ounce, and fresh vegetables (sweet potatoes), 10 ounces.

This diet and its relation to deficiency disease have been described elsewhere.[2] It is not necessary to go into the matter again here, for the prevalence of xerophthalmia is sufficient to prove a deficiency in vitamin A content. The points which led me to attribute this dermatosis to a deficiency of vitamin A are:

1. Of 1,000 prisoners examined at the quarterly inspection referred to at the beginning of this paper, 81 were set aside for investigation and treatment for one or more of the following conditions: night blindness, xerophthalmia and dermatosis. Many of these suffered from acne also, but none was segregated for acne without presenting one of the other symptoms. The figures are: total number of prisoners segregated, 81; number with night blindness, 71; number with xerophthalmia, 45; number with the dermatosis, 74, and number with acne, 73.

It is thus seen that in one group of prisoners, comprising about 8 per cent of the total number of inmates in these prisons, were concentrated all the cases of known vitamin A deficiency (i. e., night blindness and xerophthalmia) as well as all the cases of the dermatosis under con-

2. Mitchell, J. P.: Prison Diets and Morbidity, East African M. J. **10**:38 (May) 1933.

sideration. It is obvious, too, that most of the 74 cases of this dermatosis showed one of the accepted manifestations of vitamin A deficiency.

2. Treatment consisted of giving each of these 81 patients 1 ounce (31.1 Gm.) of cod liver oil a day. In other respects the normal routine was unchanged, and, of course, no alteration was made in the diet. The results are shown in detail later, but for the purpose of this argument I quote the following incidence of cure after nine weeks: night blindness, 100 per cent; xerophthalmia, 100 per cent, and dermatosis, 98.7 per cent.

The known constituents of cod liver oil are: vitamin A, vitamin D and a group of fats and fatty acids of various degrees of saturation.

(*a*) That vitamin D is not the offender is fairly obvious; it is synthesized by the action of sunlight on ergosterol, and the high rate of absorption of actinic rays by the melanin-rich skin of the African makes the occurrence of rickets practically unknown among uncivilized African communities.

(*b*) A deprivation of fat only can be shown not to cause this dermatosis. In Kampala there is a prison, controlled by the native administration, in which the diet consists exclusively of sweet potatoes. A complete examination of the skins of the 250 inmates of this prison revealed a far from ideal condition, dermatologically. Dry skins were common, and scabies and other parasitic diseases were almost universal, but the dermatosis that I have described was not seen in a single case. Further, a careful inspection of the prisoners' eyes was carried out, and no cases of xerophthalmia were noted, nor was night blindness complained of. Thus, on an almost fat-free dietary which is rich in vitamin A content, a dry skin may occur, but the papulofollicular dermatosis is not seen. Incidentally, the inmates of the Central Prisons receive a fair amount of vegetable fat in their diet.

(*c*) This leaves vitamin A, and the evidence given seems to show that either this or some other so far undiscovered fat-soluble substance is the curative factor in the dermatosis.

3. During the past four months I have seen 2 cases of this dermatosis outside of prison, in the course of hospital routine. The first patient was admitted for dysentery, and during my examination I noticed several papules identical with those which I have described. The patient denied having been in prison recently, and the wage that he was earning seemed to preclude the idea of dietary deficiency. I examined his eyes, nevertheless, and found that xerophthalmia was present in both. On then inquiring into the details of his diet, it transpired that he lived on cassava only, and thus saved money for finery. Both the xerophthalmia and the cutaneous lesions cleared up promptly under treatment with cod liver oil.

The second patient whom I was asked to see had advanced xerophthalmia, dysentery and dermatosis. He was, and still is, mentally subnormal, and no history of his previous diet could be obtained. On treatment with intensive doses of cod liver oil and a diet rich in vitamin A a slow improvement in his general condition took place, so slow that I suspected an impairment of liver function and consequent failure to absorb and store vitamin A. His serum reaction was double positive, and a course of neoarsphenamine in cautious doses, combined with sodium thiosulphate, was given. At the present time his general condition is good and his cutaneous lesions have disappeared, but there is only slight improvement in the ocular condition.[3]

4. A small supply of an extract of vitamin A was obtained and given to 2 patients in daily doses of 6 minims (0.37 cc.). At the same time the sweet potato portion of their diet—the only vitamin A container—was omitted, and both were placed under rigorous dietary supervision. Xerophthalmia and night blindness cleared up promptly in both cases. The dermatosis was cured in eight weeks in one case and was almost cured in seven weeks in the other, when the supply of the vitamin A extract avoleum gave out.

5. During an inspection of 300 of the inmates of Nairobi Prison, carried out during my stay there at the time of the Centenary Meeting, 30 cases of xerophthalmia were discovered. The proportion of patients suffering from xerophthalmia, night blindness and the dermatosis was found to be precisely the same as that obtaining in the Uganda Prisons.[4]

The following data were observed in the patients under treatment: average age, approximately 35; average duration of stay in prison, twenty-six months; longest period, seventy-eight months, and shortest period, three weeks. The prisoners were drawn from all parts of the country, and no especial tribal predisposition was noted. Their habitual diet prior to imprisonment consisted of sweet potatoes, green plantains, maize and other flours and occasionally meat. The incidence of the various manifestations was as follows: total number of patients observed,

3. Owen, H. B., and Hennessey, R. S. F.: Tr. Roy. Soc. Trop. Med. & Hyg. **25**:367, 1932.

4. Dr. J. P. Mitchell and I went to Nairobi Prison not expecting to find any cases of vitamin A deficiency. We knew that the prisoners' diet contained ghee, and in the works of reference then available (Leitch, J. Neil: Dietetics in Warm Climates, London, Harrison & Sons, 1930), ghee was marked as a triple plus vitamin A container. The most recent work on this subject (Vitamins: A Survey of Present Knowledge, Medical Research Council, Special Report Series, no. 167, London, His Majesty's Stationery Office, 1932) assesses ghee as "O to single plus" only, and this explains our findings at Nairobi Prison, where, despite a daily ration of ghee, the same percentage of vitamin A deficiency occurs as in the Uganda Central Prisons.

81; number with night blindness, 71; number with xerophthalmia, 45; number with the dermatosis described, 74, and number with acne, 73. As already stated, treatment consisted solely of the administration of 1 ounce of cod liver oil to each man, in two daily doses of half an ounce each after meals.

The group of 81 patients was examined weekly, and alteration in any of the conditions noted. Cure was effected in from one to nine weeks. Represented graphically, this gives a rapid curve for the cure of night blindness, almost as steep a curve for xerophthalmia and slower ones for the dermatosis and acne.

Apart from the detailed improvement noted, this group of prisoners showed a rapid and marked improvement in their general condition. Their skins became oily and gleaming, and many volunteered the statement that they felt fitter than before. They contrasted markedly with the remaining prisoners, many of whom were on the borderline of clinical vitamin A deficiency. Actually, at a general inspection held one month after the time the original cases were discovered, 47 more cases were picked out, divided into sections as follows: night blindness, 42; xerophthalmia, 23; dermatosis, 30, and acne, 36. The average previous stay of these men in prison had been thirty-one months, and it is an interesting fact that of those who were segregated for any variety of avitaminosis A, only 10 per cent had been in prison for less than a year. The 2 cases of incidence within one month of entry into the prison were both in the juvenile section (boys about 15 years of age).

COMMENT

The medical literature has so far been remarkably reticent regarding the changes in the skin in avitaminosis. The only attempt that I can find at a meticulous description of the lesions is that of Pillat,[1] whose paper Dr. H. B. Owen abstracted for me. Pillat's cases and mine, however, agree in only a few particulars. In both the skin is dry and scaly, and in both there are comedones on the face and chest. Here, however, the resemblance ceases; Pillat's *dermomalacie* is a decay, associated with a diminished resistance to pyogenic bacteria and consequent multiple abscesses. The condition in my cases is a dyskeratosis, with changes consequent on this condition and without signs of sepsis or softening.

It must be remembered when comparing the two sets of cases that we are dealing with different races. Pillat's patients were Chinese; mine are African. Further his patients were seen in private practice (one, at least, was of the coolie class), and there is no means of knowing whether they had been accustomed to frequent washing. Mine were all prisoners, and had a daily bath with soap.

What, then, are the true dermal manifestations of vitamin A deficiency? Though always alluded to as the anti-infective factor, there is little evidence of detail that vitamin A subserves such a function in man. The formation of leukocytes, bacteriolysins, precipitins, etc., seems to continue normally in spite of an avitaminosis.[5] It is probable that the infections which occur in some cases of vitamin A deficiency are due to breaches in epithelial surfaces permitting a more than normal invasion of bacteria, with which the body's normal defense mechanism is unable to cope. If Pillat's patients were subject to general undernourishment as well as to a specific deficiency in vitamin A, this would explain the differences between our findings. My cases would then represent the dermatosis of vitamin A deficiency, while his would have superimposed the results of general undernourishment, a possible deficiency in other accessory food factors and long-standing neglect.

Be that as it may, I can still hope that the unique experience that I have had in studying the pure avitaminosis may be of some value to future investigators.

The Director of Medical and Sanitary Services, Uganda Protectorate, gave permission to publish this paper. The officials of His Majesty's Central Prisons, Uganda, granted me facilities in this investigation. The authorities in Nairobi, Kenya Colony, permitted, and aided in, the examination of their prisoners and the demonstration of typical cases at the Centenary Meeting.

5. Hennessey, R. S. F.: Tr. Roy. Soc. Trop. Med. & Hyg. **26**:55, 1932.

Clinical Notes

FORMULA FOR A NEW LOTIO SULPHURATA

Preliminary Note

E. William Abramowitz, M.D., New York

For many years a preparation known as lotio sulphurata alba has been employed for the treatment of acne, rosacea and allied conditions that require some stimulating, keratolytic and astringent action. The mixture is prepared with 4 or 8 cc. each of a saturated (1½ : 1) solution of zinc sulphate and a saturated (1 : 2) solution of sulphurated potassa in 100 cc. of rose water. Frequently it is necessary to increase the amount of these active ingredients fourfold. The stronger preparation is known as lotio sulphurata concentrate. It is not easy to make up unless the pharmacist has had special experience with its preparation.[1] This is particularly true of the concentrated preparation.

Several months ago, in preparing lotio sulphurata concentrate, a druggist, instead of taking the sulphurated potassa solution that he had on hand, by mistake added solution of sulphurated lime (Vleminckx's solution) and in this way inadvertently showed a new way of preparing lotio sulphurata.

I have tried the new preparation in a number of cases of acne and rosacea and have found that it possesses some definite advantages over the old lotio sulphurata. It is just as easy to apply and is much more readily removed. A preparation made three months ago is still in good condition, whereas the first type of lotio sulphurata concentrate of that age would be too dry to use. The newer compound can be made easily; the appearance is that of a smooth, white, gritless mixture of the consistency of greaseless cream.

In order to avoid an excess of the active ingredients, a proper proportion was established by calculated composition with the resulting formula. This was prepared with the help of Dr. E. F. Williams of the department of biochemistry of the New York Post-Graduate Medical School and Hospital. The prescription is as follows:

Solution of sulphurated lime, N. F. (filtered)	30 cc.
Saturated (1½ : 1) solution of zinc sulphate in rose water (filtered)	20 cc.
Glycerin	5 cc.

From the Department of Dermatology and Syphilology of the New York Post-Graduate Medical School and Hospital, Columbia University.

1. Raubenheimer, Otto: Lotio Alba, J. Am. Pharm. A. **3**:692 (May) 1914. Peacock, J. C., and Peacock, B. L. De G.: Some Notes of an Interesting Prescription (Lotio Alba), Proc. Pennsylvania Pharm. A., 1914, p. 256.

Weaker concentrates may be secured without further difficulty by the addition of larger amounts of rose water. After the reaction caused by mixing these ingredients subsides, an analysis shows the following constituents:

	Percentage
Zinc sulphide	8
Sulphur (amorphous)	5
Calcium sulphate	12
Calcium thiosulphate	6
Water	69
	100

My associates and I are now using the mixture at the skin clinic of the Post-Graduate Medical School and Hospital and we are studying the rationale of the compound as based on its individual components. We hope that others will use it to test its value. A more detailed report will be submitted if continued good results warrant.

853 Seventh Avenue.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

MULTIPLE BENIGN EPITHELIOMA OF THE SCALP. F. RONCHESE, Am. J. Cancer **18**:875 (Aug.) 1933.

Under this title and the descriptive term "turban tumor" the author presents a comprehensive case report and a review of the literature regarding a condition which is commonly designated as endothelioma capitis or cylindroma of the scalp. He defines the condition as a multiple, benign, familial, nodular, turban-like, basal cell epithelioma of the scalp, with cylindromatous degeneration. The lesions appear to arise from the epithelium of the sebaceous glands and bear a definite relationship to adenoma sebaceum and epithelioma adenoides cysticum. The nodules appear singly or multiply in adolescence or in early adult life; they occur more commonly in females and increase in numbers and enlarge in size. Diagnosis is based on the large number of lesions and their slow growth, varied size, firm, rubber-like consistence, pink or bluish hue and lobulated or pedunculated shape. Removal of a few tumors at a time with the cutting current or scalpel is advocated in preference to treatment with roentgen rays or radium, which appear ineffectual.

THE RÔLE OF SODIUM, POTASSIUM, CALCIUM AND MAGNESIUM IN CANCER. M. J. SHEAR, Am. J. Cancer **18**:924 (Aug.) 1933.

The author summarizes a ninety-four page review with the statement that sodium appears to have neither an inhibiting nor an accelerating effect on the growth of tumors, that potassium may have a stimulating effect, while calcium may have a very slight retarding effect, and that magnesium does not appear to have the inhibitory effect that has repeatedly been claimed for it. This type of research has not yet advanced to the point where it can be applied practically in therapy.

MULTIPLE HEMANGIOMAS SHOWING CERTAIN MALIGNANT CHARACTERISTICS IN AN INFANT. A. C. TAYLOR and E. MOORE, Am. J. Cancer **19**:31 (Sept.) 1933.

The authors preface their article with the remark that a survey of the literature indicates that multiple hemangiomas are not uncommon in various organs. They report a case of multiple hemangiomas in an infant, in which the skin, liver and lungs were involved. The invasion and destruction of hepatic tissue by the hemangiomatous growth and the appearance of scattered hemangiomatous nodules in the lungs, which were possibly of a metastatic type, suggested potential malignancy, though the cellular changes characteristic of malignancy were not observed.

H. R. FOERSTER, Milwaukee.

LYMPHOGRANULOMATOSIS VENEREA. W. E. COUTTS, J. MARTINI HERRERA and F. LANDA PERRONI, Am. J. Surg. **21**:96 (Oct.) 1933.

The authors briefly review the historical aspects of the disease. As a result of their investigations, they believe that the virus that causes lymphogranulomatosis is of buccal origin, and that coitus analis is responsible for the rectal syndrome seen in the condition. They believe that all of the conditions which fall under Durand, Nicolas and Favre's denominations are not one and the same disease for the following reasons: Of eighty-two men presenting subacute inflammation of the inguinocrural and deep iliac lymph nodes, thirty-two showed no external

lesion to explain the lymphatic involvement. Of the thirty-two patients, the Frei test was positive in twenty-two, and the authors believe that Frei's reaction is not specific. They make a differentiation between cases of inflammation of the inguino-iliac lymph glands in which a site of inoculation can be established and those in which no primary lesions can be found. In cases in which a primary lesion is found the symptoms are as follows: Ganglionic inflammation, usually one-sided, appears a few days after the appearance of a primary lesion which is negative on dark-field examination. The lymph nodes show a marked tendency to suppurate, with the establishment of fistulas. Fever and malaise accompany the lymphatic involvement. There is frequently an associated mononucleosis with lymphopenia. In cases in which no primary lesion is found, the symptoms are as follows: The onset speaks in favor of a systemic invasion. The involvement of the lymph nodes is preceded by fever, arthralgia, malaise and general discomfort. Eosinophilia is constant. There is inflammation of the superficial lymph nodes, the deep iliac nodes and the abdominal lymph glands. The arthralgia is transitory and resembles gonorrheal arthritis. The lymph glands do not suppurate but persist as hard, scirrhus nodes for several months. The disease usually lasts for about three months, with gradual improvement in constitutional symptoms.

PERLSTEIN, Chicago.

SYPHILITIC PERIPHERAL VASCULAR DISEASE. L. G. HERMANN, Am. J. Syph. **17**:305 (July) 1933.

The author describes three types of peripheral vascular disturbances due to syphilis: the angiospastic type, the endarteritic type and the thrombo-arteritic type.

The angiospastic type occurs in the upper extremities and manifests itself as a chronic arteriospasm associated with constant pain in the distal parts of the affected extremity. It is the result of periarteritis of the smaller or medium-sized vessels which produces chronic irritation of the perivascular plexus of nerve fibers, giving rise to reflex vasomotor disturbances in the form of chronic vasospasm. An illustrative case is reported.

The endarteritic type is most commonly seen in the legs and feet and manifests itself by constant pain, intermittent claudication and evidence of organic obliteration of the arteries. A case of a condition which the author believes can be designated clinically as syphilitic endarteritis obliterans is reported.

The thrombo-arteritic type is uncommon. It manifests itself by extensive organic occlusion of all the major arterial pathways of the extremities, without evidence of gross gangrene. A case is presented which illustrates this type of syphilitic peripheral vascular disease.

In regard to treatment, active antisyphilitic treatment plus care of the skin to prevent infection is of primary consideration. After the antisyphilitic treatment has arrested the progress of the disease, the patient should be given the benefit of any further collateral circulation that can be brought about by the use of the intermittent negative pressure environment for the affected extremities. The apparatus and the technic used to produce an intermittent negative pressure environment are described. The author believes that this method is the most effective means of bringing about the development of an adequate collateral circulation in extremities with an extensive obliterative arterial disease, regardless of the cause.

A METHOD TO INTRODUCE LARGER AMOUNTS OF THE ARSPHENAMINES INTO THE CENTRAL NERVOUS SYSTEM. J. WITTENBERG, Am. J. Syph. **17**:339 (July) 1933.

As drugs of the epinephrine series are powerful dilators of the cerebral vessels in man, and as the bulk of arsphenamine injected intravenously is deposited in the tissues in a few minutes, it was thought that by taking both these facts into consideration and by proper timing an increased amount of arsphenamine could be introduced into the central nervous system. The author reports on a small

number of patients who were treated by the intravenous injection of ephedrine followed within two minutes by the intravenous injection of neoarsphenamine. The treatment is safe with properly selected patients, and a larger amount of arsenic is found in the cerebrospinal fluid following this modified form of treatment than is the case with the method generally used. This method is worthy of further study.

THE REACTION OF SPIROCHETA PALLIDA, RECURRENTIS AND TRYPANOSOMA EQUIPERDUM TO ARSENOBENZOL PREPARATIONS. F. FÖLDVÁRI, Am. J. Syph. **17**:346 (July) 1933.

The author observed that by impregnation a part of the arsphenamine preparations is tied up to trypanosomes as well as to Spirochaeta recurrentis and Spirochaeta pallida in a way as yet unknown. This fact was considered of no value, because it was thought that previous fixation with methyl alcohol had probably produced a changed condition in the germs.

However, in another series of tests, when treatment with arsphenamine was applied without previous fixation with methyl alcohol, the germs became similarly impregnated. This evidence seems to show that arsphenamine preparations are taken up by the germs. Impregnation after previous treatment with parafuchsin seemed to interfere with the intensity of impregnation, as compared with the results obtained without previous treatment with parafuchsin. This, perhaps, might serve as proof for the thesis that arsphenamines are taken up by the trypanosomes and that the albumin contained in their bodies reacts with the arsphenamine owing to its affinity for the latter.

THE IRON REACTION IN PARETIC NEUROSYPHILIS. H. MERRITT, M. MOORE and H. C. SOLOMON, Am. J. Syph. **17**:387 (July) 1933.

Iron which is present in all normal brains in a fairly characteristic distribution is spoken of as endogenous iron; it is found chiefly in the basal ganglions and in the dentate nucleus. Pathologically, iron is found in the brain in two general types of diseases: In diseases in which red blood cells have been extravasated into the tissues iron pigment is found in and near the areas where the hemorrhage or hemorrhages occurred; and it is present in dementia paralytica, in which it is known as *Paralysecisen*, or the iron of dementia paralytica. It is found in a very characteristic manner: When brain tissue is stained with Turnbull's blue, small spicules of iron pigment are found in the cells of the walls of the blood vessels and in the body or processes of the microglia cells. This iron is distributed diffusely through the cortex, basal ganglions and other regions of the brain. Many authors believe that an absolute diagnosis of dementia paralytica can be made from the iron reaction. In meningitis, multiple sclerosis and other neurologic disorders deposits of pigment are not found, and even in the study of brains in which hemorrhage has occured confusion is not likely, because in these brains the iron is found in circumscribed areas. In nonparetic neurosyphilis, deposits of iron are usually absent. In slowly developing or in stationary cases the iron reaction is commonly very weak, and at times one may miss it.

The source of the iron pigment is not clear. As dementia paralytica is the example par excellence of spirochetal infection of the brain, and as it is the only disease in which this form of iron is found, it would seem logical to conclude that the presence of iron is closely related to the primary nature of the pathologic process.

WASSERMANN REACTION IN UNTREATED SYPHILIS. E. T. HOVERSON, G. W. MORROW and R. O. HAWTHORNE, Am. J. Syph. **17**:392 (July) 1933.

The records of fifty-nine untreated patients who gave a positive Wassermann reaction on admission to the Kankakee State Hospital were examined. Eighteen, or 30.5 per cent of these patients, gave a negative Wassermann reaction after an

average length of stay in the institution of ten and two-tenths years. It is concluded that a reversal of the positive serologic finding to negative findings occurred in these patients without any antisyphilitic treatment. REUTER, Milwaukee.

CALCINOSIS UNIVERSALIS. BARNEY J. HEIN, Arch. Surg. **26**:389 (March) 1933.

A case of diffuse deposition of calcium in the fasciae is presented in a child, aged 6½ years. There were indurated areas in the upper and the lower extremities. Roentgen examination showed calcareous deposits in various parts of the body. The blood calcium was 16 mg. in February, and 10 mg. in August. The child recovered with the use of heliotherapy, and progressive roentgenograms showed a gradual disappearance of the calcium.

KAISER, Rochester, N. Y. [AM. J. DIS. CHILD.]

THE REACTION OF STANDARD BREEDS OF RABBITS TO EXPERIMENTAL SYPHILIS. P. D. ROSAHN, J. Exper. Med. **57**:907 (June) 1933.

The conclusions drawn from the experimental work on the response to syphilitic infection were that standard bred Havana and Dutch rabbits were resistant to infection, while English, Himalayan and Rex rabbits were susceptible.

STUDIES ON INFLAMMATION: IX. A FACTOR IN THE INVASIVENESS BY PYOGENIC BACTERIA. V. MENKIN, J. Exper. Med. **57**:977 (June) 1933.

Inflammatory irritants, when injected into tissues, rapidly form a mechanical barrier in the form either of coagulated plasma or of thrombosed lymphatics, or of both. Staphylococci were found to stop the draining of dye into tributary lymphatics when the dye was injected as early as one hour after the injection of the micro-organisms. Pneumococcus type I, used to produce cutaneous inflammation, caused the injected dye to be retained when it was injected after six hours or later. In the case of Streptococcus haemolyticus, the dye drained readily for the first thirty hours after the inflammatory reaction began. After the inflammation was of forty-five hours' duration, the dye remained fixed. JAMIESON, Detroit.

AN OUTBREAK OF DERMATITIS IN COTTON MILLS DUE TO VARNISH. LOUIS SCHWARZ and CHARLES L. POOL, J. Indust. Hyg. **15**:214 (July) 1933.

In nineteen of thirty-two workers exposed to varnish on heddle frames dermatitis of the hands and forearms developed after from three days to four weeks of contact with the varnish. In twelve of thirteen patients, patch tests with the varnish gave positive results. Of the twelve who were found to be sensitive to the varnish, eight were tested further with various ingredients of the varnish. Two showed sensitivity to cumaron resin and ceresin; one was sensitive to resin only; four were sensitive to ceresin but not to the cumaron resin, and one was sensitive to neither alone but reacted positively to the varnish containing them. The varnish of the frames was more irritating than dried fresh varnish, probably because of the hydrochloric acid given off by the ceresin containing chlorine after long standing. The cumaron resin contained sulphuric and sulphonic acids. The addition of physiologic solution of sodium chloride to the materials tested for the purpose of stimulating perspiration added to the irritating action of these substances in susceptible persons.

THE RELATION OF CARCINOGENICITY OF MINERAL OILS TO CERTAIN PHYSICAL AND CHEMICAL CHARACTERISTICS OF THESE OILS. R. LYTH, J. Indust. Hyg. **15**:226 (July) 1933.

The author determined the refractivity of a large series of mineral oils which had been previously tested for carcinogenic properties, as well as the iodine values and permanganate oxidation values. He found that, with the exception of

Pennsylvania oils, the refractivity of an oil is a good index of its carcinogenic strength: Oils with a value of 0.56 and over are very toxic, while those under 0.55 are nontoxic; oils with values between these vary in general in toxicity, those of lower value being relatively nontoxic, while those of higher value are likely to be toxic but are not necessarily so. Toxicity varies similarly with iodine value, if the oils have not been treated; if the value is above 26, the oil is likely to be toxic, and if the value is above 30, it is almost certain to be so. In treated oils the toxicity is apt to be reduced disproportionately to the difference in iodine value. The permanganate oxidation values are not indicative of the carcinogenic properties of the oils as determined by the method employed by the author.

WIEDER, Milwaukee.

RINGWORM OF THE TOES IN STUDENTS AND DISPENSARY PATIENTS. EMANUEL MUSKATBLIT, New York State J. Med. **33**:632 (May 15) 1933.

Muskatblit found, on examination for ringworm of the toes of 100 dispensary patients and 112 medical students unselected, that in 89 per cent of the 212 cases there were more or less pronounced changes of the skin in the toe-webs, mostly of macerative type, suggestive from the standpoint of mycotic infection.

Fungi were found microscopically or in cultures in 31.6 per cent of all cases examined. The percentage was higher in students (34.8) than in dispensary patients (28).

Microscopic examination alone was positive in 27 per cent of all the cases. This percentage increased to 31.4 when clinical changes in the skin were present, and reached 47.4 in the group of patients with marked lesions of the skin. Two types of fungi could be distinguished in microscopic preparations: true hyphomycetes and yeastlike fungi.

Cultures were positive in 17.9 per cent of all cases, in 50.8 per cent of microscopically positive cases and in 5.2 per cent of microscopically negative ones. No fungi were found either microscopically or culturally in clinically healthy persons.

LICHENOID SARCOID (BOECK): REPORT OF A CASE WITH REVIEW OF THE LITERATURE. JOSEPH L. MORSE, New York State J. Med. **33**:686 (June 1) 1933.

Reports on ten cases of Boeck's sarcoid with lichenoid lesions were found in the literature and reviewed. In only two cases, those of Wright and of Kissmeyer, were there lichenoid lesions alone without other lesions typical of sarcoid. The diagnosis in these cases can be positively established only after careful histologic study, but in clinically atypical lichenoid eruptions this form of sarcoid should be kept in mind. A case of this type which responded to treatment with gold sodium thiosulphate given intravenously is reported.

SQUAMOUS CELL EPITHELIOMATA OF THE SKIN OF THE FACE. EUEGNE F. TRAUB and JESSE A. TOLMACH, New York State J. Med. **33**:875 (July 15) 1933.

Squamous cell epithelioma of the face not involving the mucous membrane surfaces has received little or no attention in dermatologic textbooks, and, usually, has not been recognized clinically in the early stages. The lesion examined was of a type not as infrequent as had been generally supposed. It presented a very definite and readily diagnosable picture. Twenty-six cases with follow-up histories are reported in detail. The rapid early development of the lesion is stressed as compared to that of a basal cell growth. In five cases there was a history of trauma preceding the appearance of the nodule. In nine cases, the lesion was removed by a wide excision with an endotherm knife alone, and in eight cases this was combined with irradiation of the base. Treatment by radium alone was given in one case and by roentgen rays alone in one case, and endothermy was performed with a knife in seven cases. Twenty-one of the cases showed excellent

cosmetic results and apparent cures after periods of observation ranging from two months to five years. Thirteen patients have remained well for at least two years. In no case has wide removal been followed by local return of the lesion, and yet the cosmetic results were quite satisfactory. In none of the cases, apparently, have the lymph nodes draining the affected areas been involved. Irradiation was not practiced before removal, but in the early cases of this group, removal of the lesion was immediately followed by either roentgen or radium therapy. As this procedure delayed healing and seemed to be of no distinct advantage in adequately removed lesions, it has been discontinued.

TOXIC ACTION OF METALS IN ALOPECIA AREATA. C. N. MYERS, BINFORD THRONE and JEROME KINGSBURY, New York State J. Med. **33**:991 (Aug. 15) 1933.

The authors believe that as a result of their studies the "toxic theory" of causation of alopecia areata is further substantiated. Twenty-nine per cent of the patients with alopecia areata showed abnormal determinations of basal metabolism; 71.83 per cent of the cases showed lymphocytosis; 75.75 per cent of the urines examined showed the presence of metals (arsenic, lead). The elimination of diseased teeth, tonsils, sinuses or other toxic possibilities, including the metals, resulted favorably in the restoration of the hair in the majority of the cases. In patients with a lowered basal metabolic rate glandular therapy was added to the treatment.

TRAUB, New York.

ARSPHENAMINE DERMATITIS. A. G. SCHOCH, Texas State J. Med. **29**:372 (Oct.) 1933.

In seeking to explain the pathogenesis of postarsphenamine dermatitis, one school of thought holds that it results from toxemia produced by the arsenic, whereas another insists that it rests on the basis of an acquired allergic state—a specific sensitization to arsphenamine. However, neither the toxic nor the allergic hypothesis satisfactorily explains all of the phenomena associated with the dermatitis, and it is most likely, this writer feels, that both mechanisms play a part, one or the other predominating in varying degrees in the given case.

The allergic type, he claims, is not a disease of the skin per se, for it affects other systems as well. The blood picture frequently shows leukocytosis, eosinophilia and a low nuclear index.

A recurrence of the dermatitis can now most certainly be foretold by use of the patch test, a positive reaction being an absolute contraindication to further arsphenamine therapy.

GANDY, Houston.

INDUSTRIAL ANTHRAX. F. W. ENRICH, Brit. M. J. **2**:50 (July 8) 1933.

The author's observations are based on 340 cases of cutaneous anthrax and 24 cases of pulmonary and gastro-intestinal anthrax, which occurred in Bradford, the chief center of industrial anthrax in Great Britain. Cutaneous anthrax is seen most frequently on exposed parts, but the skin of the fingers is rarely attacked. In tanners, the neck is a frequent site, and lesions have been noted on the shin, thigh, abdominal wall and chest. The diagnosis is primarily bacteriologic; the malignant pustule usually considered typical of anthrax only can be simulated by a vaccine pock or a streptococcic or pneumococcic infection, and in 1 case the hay bacillus gave rise to a similar lesion. Aberrant forms are not infrequently seen. Instead of the coal-black central eschar surrounded by a ring of vesicles on an angry, red and brawny base, there may be an eschar only; bullae may predominate, or white edema may replace the red area. In 1 case, in which the lesions occurred on an arm, the edema was so extensive as to disfigure the part. Microscopic examination is usually sufficient, so it is a mistake to withhold specific treatment for cultural confirmation. Treatment is by the injection of arsphenamine

and antianthrax serum. Two moderately large doses of arsphenamine are given at an interval of a day, and two injections of serum are given intravenously or subcutaneously—80 cc. the first day, followed by 60 cc. the next day. A total of 300 cc. of serum has been given with no ill effects. The affected parts must be put at rest. Treatment by excision has been abandoned. With this method the results have improved so that among the last 200 patients treated the mortality rate has been only 5 per cent. The prognosis depends largely on an early diagnosis. Systemic anthrax is briefly considered, and the article contains also an interesting paragraph on unusual sources and modes of infection.

THE TREATMENT OF RODENT ULCERS. N. S. FINZI, Brit. M. J. **2**:137 (July 22) 1933.

The treatment recommended is a mild erythema dose of filtered radium, to be repeated after six weeks if any evidence of growth visible to the naked eye remains. Then, at intervals of six and fourteen weeks after the last curative dose, two prophylactic doses are given. With this method the author has obtained cure in 99 per cent of early cases; statistics are not furnished. It is only when dealing with "other people's failures" (i. e., unfiltered or lightly screened radiations) that the results are not so good. Dr. Roy Ward and Dr. A. J. Durden Smith (*Brit. M. J.* **2**:212 [July 29] 1933) challenge the last statement of Dr. Finzi. In a series of about 1,700 consecutive cases they had the best results from a single application of unscreened radium. Dr. R. T. Brain also protests against Dr. Finzi's criticism of unscreened radiation. It is his experience that results obtained with gamma ray therapy seemed to be better than those obtained with the unscreened plaque, but careful analysis shows this to be more apparent than real. This applies to superficial lesions; older cases require adequately screened irradiation.

OCCUPATIONAL DERMATITIS. W. G. HARVEY, Brit. M. J. **2**:321 (Aug. 19) 1933; OCCUPATIONAL DISEASES OF THE SKIN. JOHN C. BRIDGE, ibid., p. 324.

These two excellent articles deal with the subject generally. The first article contains a full summary of the literature; the second is concerned rather with the industrial point of view and is chiefly a statistical study. Harvey believes that dermatitis and eczema should be regarded as synonymous terms. He discusses in detail bakers' dermatitis and dermatitis caused by dyes, especially as to pathogenesis. He considers the former to be a disease in which a series of injuries have a cumulative effect and act like eczematous irritation. Bridge discusses more fully the prophylactic measures which are employed in industry. The articles are both source papers and should be read, as they do not lend themselves to abstracting.

EPITHELIOMA OF RODENT TYPE IN A NATIVE OF BOUGANVILLE, TERRITORY OF NEW GUINEA. C. MERVYN DELAND, L. B. BULL and J. B. CLELAND, M. J. Australia **1**:712 (June 10) 1933.

The interest of this case is in the great rarity of such a growth on a black skin, the presence of granules of melanin pigment in some of the tumor and stroma cells and the age of the patient, 30 years.

RATTNER, Chicago.

FAVORABLE INFLUENCE OF EXFOLIATIVE DERMATITIS COMPLICATING PSORIASIS. GOUGEROT and PATTE, Bull. Soc. franç. de dermat. et syph. **40**:106 (Jan.) 1933.

A patient with widespread psoriasis of long standing was cleared of lesions by the intervention of an acute generalized exfoliative dermatitis, and the authors point out the analogy between this case and the favorable influence exerted on syphilis by postarsphenamine dermatitis.

NATURE OF LICHEN PLANUS. M. G. MILIAN, Bull. Soc. franç. de dermat. et syph. **40**:114 (Jan.) 1933.

Various arguments which are set forth in favor of the view of a close relationship between lichen planus and tuberculosis may be summarized as follows: (1) the occurrence of familial and conjugal lichen planus; (2) the histologic resemblance between the two diseases; (3) the response of lichen planus to therapeutic agents used in the treatment of tuberculosis (e. g., gold, neoarsphenamine and ultraviolet rays); (4) the frequently noted appearance of lichen planus, or lichen planus-like lesions, after treatment with a gold compound in tuberculous conditions, which suggests a biotropic eruption of tuberculous nature; (5) positive tuberculin reactions in lichen planus; (6) the clinical resemblance between tuberculous lesions and those of lichen planus (e. g., lichen corne and verrucous tuberculosis and lichen nitidus and tuberculids).

POSTARSPHENAMINE NITRITOID CRISIS AND PURPURA. SEZARY and A. DURUY, Bull. Soc. franç. de dermat. et syph. **40**:131 (Jan.) 1933.

A young woman with early syphilis was given a course of ten injections of bismuth and neoarsphenamine concurrently. Several days after the last injections a purpuric eruption developed on the lower extremities, accompanied by gingival hemorrhages. Eight months later a hematologic examination showed no abnormalities; therefore, a second course of treatment was begun. A single injection of 15 cg. of neoarsphenamine immediately provoked a violent nitritoid crisis followed four hours later by a new outbreak of purpura and hemorrhages, similar to the first. The only anomaly of the blood found was irretractability of the clot, a common finding in many conditions, and therefore of small significance here. It is well known that postarsphenamine purpura is generally a late accident and nearly always accompanied by gross changes in the blood. The suggestion is advanced by the authors that the cause of the nitritoid crisis and of the purpura in their patient was probably identical, namely, a marked vasodilatation of the capillaries of the skin brought on by some perturbation of the sympathetic system which precipitates first the nitritoid crisis and then the purpura.

GANDY, Houston, Texas.

NEVUS SEBACEUS OF THE FACE. E. REDAELLI, Gior. ital. di dermat. e sif. **74**:122 (Feb.) 1933.

The author reports a case of sebaceous nevus situated on the left side of the forehead and on the left cheek. Differential diagnosis with adenoma sebaceum is considered. Histopathologic examination showed the lesions to be composed of huge lobuli of sebaceous glands of apparently normal structure.

POSTARSPHENAMINE PSORIASIS. L. CIARROCCHI, Gior. ital. di dermat. e sif. **74**:149 (Feb.) 1933.

Ciarrocchi reports a case of psoriasis vulgaris which appeared suddenly in a patient with syphilis after the sixth dose of neoarsphenamine. On the basis of his investigations of the endocrine system of this patient, Ciarrocchi concludes that the condition was due to an early syphilitic involvement of the thyroid gland, aggravated by the biotropic action of neoarsphenamine. The patient recovered entirely under thyroid therapy and on the continuation of injections of arsphenamine.

PARDO-CASTELLO, Havana, Cuba.

RAYNAUD'S DISEASE IN AN EIGHT YEAR OLD CHILD. MARTIN GONZALEZ-ALVAREZ, Pediatría españ. **22**:97 (Feb.) 1933.

Raynaud's disease, which is so rare in childhood, occurred in a child of 8 years. The first symptoms appeared at the age of 6 and began with severe pain in the affected extremities. The pain was followed by inflammatory manifestations

and edema. Rose-colored, wheal-like spots were general over the body. The skin was very dry. Infarcted areas developed proximal to the painful regions. The lesions at times showed regression of symptoms followed again by exacerbation. The Mantoux reaction was strongly positive. The Wassermann reaction was negative. The typical picture of Raynaud's disease with loss of three end phalanges of the right hand and two of the left hand finally developed.

The roentgenologic thoracic findings indicated extensive tuberculous involvement. Application of both dry and moist heat gave relief to the extreme pain in the affected extremities.

The author advocates roentgen therapy over the suprarenal regions. The ultimate prognosis in these cases is very grave.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

THE CHEMICAL INVESTIGATION OF PSORIASIS. BERNHARD ZORN, Dermat. Wchnschr. **96**:89 (Jan. 21) 1933.

The scales from an untreated patient with psoriasis were collected and freed as much as possible from extraneous matter, such as blood and hair. They were then submitted to a detailed quantitative chemical examination. The findings are summarized in the following tabulation:

	Water-Containing Scales, Mg. Per 100 Gm.	Water-Free Scales, Mg. Per 100 Gm.
Nitrogen	13,160	14,490
Calcium	136	150
Magnesium	27.5	30.3
Sodium	644	709
Potassium	306	337
Phosphorus	15.1	16.6
Total halogens	309.8	341
Iodine	Not demonstrable	Not demonstrable
Sulphur	855.3	941.3

CHOLESTEREMIA IN LUPUS ERYTHEMATOSUS. B. W. JLINSKY, Dermat. Wchnschr. **96**:739 (June 3) 1933.

In a series of thirty-three patients with lupus erythematosus, Jlinsky found that the cholesterol content of the blood averaged a little higher than that in normal patients.

SCARLET FEVER. KURT SCHIRLITZ, Dermat. Wchnschr. **96**:746 (June 3) 1933.

The author reviews the 106 cases of scarlet fever seen during the first nine months of 1932. The complications encountered were: disease of the kidneys, 53 per cent; disease of the ears, 22 per cent; rheumatism, 17 per cent; endomyopericarditis, 5 times, and thyroiditis, paratonsillar abscess and pulmonary abscess, each once.

TROPHEDEMA OF MEIGE-MILROY. L. LEVEN, Dermat. Wchnschr. **96**:777 (June 10) 1933.

A boy, aged 19, had a localized area of edema in the region of the right heel which had been present as long as he could remember. Examination showed a feminine distribution of the hair, moderate hyperthyroidism and spina bifida. The condition was considered to be an example of Meige-Milroy disease.

AN UNUSUAL CASE OF PURPURA. EMANUEL WOHLSTEIN, Dermat. Wchnschr. **96**:783 (June 10) 1933.

A woman, aged 42, acquired polyarthritis during the course of which acute tonsillitis occurred. Later hemorrhagic nephritis and purpura appeared. The purpura consisted of purpuric, nonconfluent macules and of elevated oval, circular and ringed papules.

TREATMENT OF LICHEN RUBER PLANUS BY HYPNOSIS. A. KARTAMISCHEW, Dermat. Wchnschr. **96**:788 (June 10) 1933.

The author treated eight patients suffering from lichen planus by suggestion. He followed the method used by Bloch and others in treating warts. In four of the cases a complete cure was obtained; in three the condition was improved, and in one it was unchanged.

URIC ACID, PSORIASIS AND GOUT. BERNHARD ZORN, Dermat. Wchnschr. **96**:821 (June 17) 1933.

Fifty grams of psoriatic scales was gathered from a single patient. The uric acid content was determined to be 306 mg. per hundred cubic centimeters. The author believes that this high uric acid content explains the frequent association of gout with psoriasis.

GRENZ RAY TREATMENT OF VITILIGO. W. WOLFFENSTEIN, Dermat. Wchnschr. **96**:828 (June 17) 1933.

The author treated six patients with vitiligo by means of supersoft roentgen rays. The method followed was that of generalized irradiation as described by Bucky. The areas of vitiligo received no direct radiation. One case in which the patient showed marked improvement is described in detail, and the author reports three other cases in which the patients were definitely benefited, and two in which the patients failed to respond.

DEMONSTRATION OF TUBERCLE BACILLI BY THE METHOD OF RAMEL IN RHEUMATOID CUTANEOUS CONDITIONS AND IN LUPUS ERYTHEMATOSUS. R. M. BOHNSTEDT, Dermat. Wchnschr. **96**:865 (June 24) 1933.

Following the technic of Ramel, the author attempted to demonstrate tubercle bacilli by the transfer of urinary sediment and blood to animals in one case of erythema nodosum, in six cases of erythema exsudativum multiforme, in two cases of lupus erythematosus and in one case of lymphogranulomatosis. In no instance was a positive result obtained.

TREATMENT OF PSORIASIS WITH SODA BATHS. OTTO STEINER, Dermat. Wchnschr. **96**:909 (June 30) 1933.

The author gives in some detail a description of the method of giving soda baths to patients with psoriasis. He indicates that the treatment is of considerable value in this disorder.

OBSERVATIONS ON THE PRESENT QUESTIONS OF DERMATOMYCOLOGY: III. EPIDEMIOLOGY OF FAVUS. C. L. KARRENBERG, Dermat. Ztschr. **66**:198 (May) 1933.

Favus in Bonn and the Surrounding Region.—Between 1900 and 1932, 274 cases of favus were seen at the clinic at Bonn. There has been no marked increase in the incidence of the condition in this region. There were probably a considerable number of patients who did not come for treatment. A statistical study of the material observed is presented in the form of a number of tables. A relatively small number of cases were brought in from other localities. It appears from a study of the disease that a predisposition must be present and also that there must be exposure before a new infection occurs.

Epidemiology of Favus in Germany.—Favus is endemic in the eastern provinces and in the western part of Germany. In other regions only sporadic cases occur. In no portion of Germany is the condition so common as it is in the eastern European countries. Achorion schoenleinii is the most frequent causative agent of favus in Germany.

SEBOCYSTOMATOSIS. J. R. PRAKKEN, Dermat. Ztschr. **66**:215 (May) 1933.

The patient, a man, aged 48, had multiple tumors scattered over the trunk for thirty-six years. Histologic examination by means of serial sections showed that the tumors were sebaceous cysts containing an oily, yellow substance. They were apparently due to hyperkeratosis developing in the follicular openings of the sebaceous glands.

TREATMENT OF NEUROSYPHILIS WITH HERPES VIRUS AND OF MALARIA WITH A NONSPECIFIC PROTEIN. H. HRUSZEK, Dermat. Ztschr. **66**:230 (May) 1933.

Naegeli and others believe that the spontaneous development of herpes simplex during fever therapy influences the course of treatment favorably. In treating two patients who had positive findings of the spinal fluid, the author used malaria reenforced with a nonspecific protein, in addition to inoculations with herpes virus. Both patients had a history of spontaneous herpes simplex. In both instances an improvement of the findings of the spinal fluid was demonstrated.

RADIATION THERAPY OF HIDRADENITIS AXILLARIS. H. MEYER-BULEY, Dermat. Ztschr. **66**:235 (May) 1933.

The author discusses the theoretical and practical considerations in the treatment of infections of the axillary sebaceous gland by means of roentgen rays. He used a filter of 3 mm. of aluminum or 0.5 mm. of copper and increased or decreased the dose in accordance with the degree of inflammatory reaction.

FOREIGN BODY PEPPERING OF THE SKIN AS AN INDUSTRIAL INJURY. THEODERICH NIMPFER, Dermat. Ztschr. **66**:313 (June) 1933.

Four patients were seen with peppering of the exposed portions of the skin with minute particles. They were employed at cleaning gas pipes and meters; they used compressed air to force out the various foreign bodies, such as rust, which had accumulated over a considerable period. A varying inflammatory reaction surrounded each particle which was lodged in the skin, and many of the particles were palpable as tiny spines. In one case a biopsy was performed, and the foreign bodies were seen to lie close to the surface as if placed there by tattooing.

LATENT SYPHILIS AND THE INOCULATION OF LYMPH GLANDS. G. CHATSCHATURJAN, Dermat. Ztschr. **66**:315 (June) 1933.

The first patient was a man, aged 36, who had been treated four years previously for early secondary syphilis. The blood and spinal fluid showed negative reactions to the Sachs-Georgi and Kahn tests. Three lymph nodes were excised and injected into the testicle of a rabbit. A syphilitic chancre occurred which contained many spirochetes.

The second patient was treated three years previously for early primary syphilis. The Wassermann test of the blood and spinal fluid had always been negative. Portions of the lymph nodes injected into rabbits failed to produce a lesion.

The author points out the value of transplants of the gland in determining the presence of latent syphilis.

ETIOLOGY OF ANGIOKERATOMA OF MIBELLI. L. J. STEIN, Dermat. Ztschr. **66**:320 (June) 1933.

Two patients with angiokeratoma of Mibelli were observed, and their case histories are recited. One was a girl, aged 10 years, and the other a girl, aged 17 years. The patients had suffered from frost-bite and presented evidence of

poor circulation of the extremities as well as a family history of tuberculosis. The author reviews the various theories published as to the etiology of the condition and concludes that it is a disorder which occurs in certain tuberculous subjects who have an inherited predisposition to proliferation of the blood vessels and who are exposed to frost-bite. He does not consider it a true tuberculid.

ERYTHEMA NODOSUM EXULCERANS. EMANUEL WOHLSTEIN, Dermat. Ztschr. **66**:335 (June) 1933.

An atypical case of erythema nodosum is described in which nodules occurred over the inner malleoli of the ankles, and in which ulceration developed. The unusual features were considered to be due to the mechanical damage to which lesions in this area are subjected.

TAUSSIG, San Francisco.

NATURE OF THE TRANSVERSE MARK IN THE NAILS IN ARSENICAL POLYNEURITIS. R. WIGAND, Deutsche Ztschr. f. d. ges. gerichtl. Med. **20**:207, 1933.

In nonlethal cases of arsenic poisoning, about two months after the ingestion of the poison, all the finger-nails show a transverse, white-gray band, about 1 mm. in width (Mees mark), which finding is of great diagnostic value. The band is somewhat similar to that observed in thallium poisoning, and contains ten times as much arsenic as the apparently normal parts of the same nail. The Mees mark represents a deposit of arsenic owing to impregnation of the nail substance.

E. L. MILOSLAVICH, Milwaukee. [ARCH. PATH.]

SCLERODERMA AND ITS PATHOGENESIS. HANS SELYE, Virchows Arch. f. path. Anat. **286**:91, 1932.

Before describing the clinical picture of scleroderma, the author gives a historical introduction to the disease which was already known to Hippocrates and Galen. This is important because it contains the recognition of sclerema neonatorum as a different entity. In the clinical picture there are three different stages: the edematous, the indurative and the atrophic. Pathologically, the increase in connective tissue is not confined to the skin but involves the blood vessels, muscles, bone marrow and, perhaps, more or less, all the organs of the body. In addition, depositions of calcium salts have been observed by numerous observers. There are at present many theories which attempt to explain the condition, such as the vascular, nervous, traumatic, infectious and rheumatic theories and those based on the influence of cold, hyperthyroidism and hypothyroidism and on suprarenal insufficiency.

Nursing rats, aged from 7 to 14 days, were given from 5 to 10 units of parathormone for from three to four days, a total of from 15 to 40 units. Twenty per cent of the animals suffered from typical scleroderma, whereas the rest did not show any signs of disease or remained backward in growth and died with more or less nonspecific signs of disease (for the most part pneumonia). Just as in the human being, three stages could be distinguished. On the day after the second injection, the skin of the neck and shoulder began to swell and was painful. The next day the edema had disappeared, and in its place a flat, indurated plate of hard skin which increased in size during the following days could be felt. The parts of the skin involved were symmetrical; soon the hair fell out, and ulcers appeared which healed with the formation of crusts. Then the skin became movable again and thin (atrophic stage). If the injections were given for only five days, the skin returned to normal after three weeks, and after two months the fur was that of a normal animal. The histologic picture, which seems to be similar to that of scleroderma in human beings, is illustrated by several histologic sections of the skin which frequently show deposition of lime salts in the necrotic

areas. Infiltration of the nerves and small vessels of the skin and muscles with small round cells was observed in further analogy to the disease in human beings. The author therefore concludes that the experimental disease is analogous to scleroderma in human beings. He realizes, however, that there may be other factors influencing the condition, since he could produce it in only 20 per cent of the animals. He wishes to classify scleroderma with osteitis fibrosa cystica and Albers-Schönberg disease, since all of them are apparently due to hyperfunction of the parathyroid glands. The possible practical importance of this point of view is considered. An extensive bibliography is given.

SCHOENTHAL, New York. [AM. J. DIS. CHILD.]

INVESTIGATION OF PELLAGRA. V. AROUTUNOV-LANTE, Dissert. Dermat.-Venerol. Clin., State M. Inst., Azerbaidjan, Bakou, 1933.

This monograph is a study of 1,115 cases of pellagra collected during the epidemic in West Giorgia, from 1929 to 1931, and of 52 cases which the author, as a member of the Red Crescent Expedition, discovered in Bakou in 1932.

In the group studied 62.9 per cent were women; 30.8 per cent, men, and 18 per cent, children, 2 of whom were breast-fed infants aged 5 and 6 months.

One hundred and sixty-six patients were carefully studied. The blood, feces and urine were examined in all cases, and in 21 the skin was studied by the use of the microscope.

Nearly all the patients suffered from ankylostomiasis. Definite mental changes were noted in 7.8 per cent of the cases.

In 70 per cent of the cases the initial symptoms were cutaneous lesions; in 22.2 per cent, severe diarrhea; in 1.2 per cent, mental disturbance.

The essential changes in the blood consisted of decreased hemoglobin, erythropenia, leukopenia and, in most instances, a decreased color index, under 1. In the majority of cases there were from 40 to 42 per cent lymphocytes, from 19 to 44.5 per cent neutrophils and from 6 to 30.5 per cent eosinophils. The blood platelets were diminished. The minimum osmotic resistance of the erythrocytes was decreased. The erythrocyte sedimentation test was accelerated in all instances.

Erythema of the skin occurred from the middle of March to the middle of September. It was followed by hyperkeratosis and desquamation, sometimes associated with vesicles and pustules. In some of the patients the changes in the skin recurred several times during that period. Usually the back of the hands and feet and the neck were involved. Often, however, the skin of covered parts was also affected, as the chest, thighs, abdomen, axillae and genitals; sometimes the whole body showed changes in the skin.

In the most cachectic patients the pigmentation and depigmentation of the skin remained after the dermatitis cleared up.

In some cases the microscope showed considerable proliferation of the epidermis. The amount of pigment in the basal layer was not proportionate to the degree of visible pigmentation. In fact, in many instances it was diminished when compared with other cases which showed clinically less pigmentation. Also the amount of pigment in the corium was not proportionate to the degree of clinical pigmentation. The author concludes, therefore, that pigmentation in pellagra does not depend on the increase of melanin in the skin but on the pigment in the corneous layer which is increased as a result of physicochemical changes. This assumption was confirmed by the fact that, the more marked the pigmentation, the more distinct was the hyperkeratosis noted.

In the cutis there were hyaline degeneration and atrophy of the elastic fibers, perivascular infiltration, hyaline degeneration of the vascular walls and edema of the cutis and subcutis.

A deficiency in total and free hydrochloric acid and a complete achylia of the gastric juice were noted.

Following treatment with the administration of liver all the changes in the blood improved, except the osmotic resistance of the erythrocytes. The cutaneous lesions disappeared within from ten to twelve days.

The author regards deficiency in food as the cause of pellagra. Almost all of the patients had been eating spoiled maize which was gathered in an unripe state, was insufficiently dried and was stored in damp places. In such a food the vitamins are destroyed.

Other factors predisposing to pellagra are, according to the author: total exhaustion, addiction to alcohol, mental shocks and intestinal worms. All of the patients studied had intestinal worms, and almost all were addicted to alcohol.

The author is of the opinion that the sun rays are of secondary importance in producing erythema.

SPIROCHETE CONTENT OF THE BRAIN AND INTERNAL ORGANS OF SYPHILITIC RATS. K. YASUMOTO, Lues: Bull. Soc. japon. de syph. **9**:17 (Feb.) 1933.

Rats were inoculated with 0.6 cc. of the testicular emulsion of syphilitic rabbits subcutaneously at the scrotum or intraperitoneally and were killed at various intervals (within from thirty to three hundred and fifty days) after inoculation. Then emulsions of their internal organs or of their blood were injected into the backs of normal rabbits cutaneously in a quantitative manner. Inoculation with brain emulsion was successful in 50 per cent of the rabbits; with spleen emulsion in 80 per cent; with liver emulsion in 60 per cent; with testicle emulsion in 50 per cent, and with kidney emulsion in 40 per cent. Inoculation with blood gave negative results.

SYPHILITIC KERATITIS IN RABBITS PRODUCED BY BULBAR SUBCONJUNCTIVAL INOCULATION WITH SPIROCHETES AND DISTRIBUTION OF THE SPIROCHETES IN THE TISSUE. T. FUNABASHI, Lues: Bull. Soc. japon. de syph. **9**:25 (Feb.) 1933.

The upper or lower point of insertion of the rectus muscle near the limbus of the cornea was chosen as the site of inoculation. In thirteen rabbits which were inoculated at this point keratitis developed, which clinically closely resembled the keratitis produced by scarification or by injection into the anterior chamber. After an incubation period of from ten to twenty-seven days, rarely forty days, keratitis developed, the severity of which was apparently influenced by the season, for in summer a mild form usually developed. In the majority of rabbits granulomatous vegetation was also visible in the conjunctiva near the limbus of the cornea.

Ten rabbits which had been inoculated under the conjunctiva near the upper limbus of the cornea were observed during from eighty to ninety days, and then eighteen eyes were examined by dark-field illumination. During the incubation period no spirochetes were found. In the first stage of keratitis, spirochetes were found in the dull zone of the progressing ends of the capillaries in seven of fifteen rabbits. In the progressive stage, spirochetes were found in all the rabbits in greater numbers. They were particularly numerous in the dull zone which extended in tonguelike formation from the edge toward the pupillary region. At the height of the disease spirochetes were found in any place where proliferation of capillaries took place. In the mild form of keratitis, which was of short duration, spirochetes were found only during a brief period and only in the progressing dull zone in the region of the ends of the capillaries. Of the rabbits which were inoculated by subconjunctival injections under the lower limbus of the cornea, only ten eyes were examined; spirochetes were found either before or after the keratitis became manifest.

BLOOM, New York.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

MAX S. WIEN, M.D., *Secretary*

Regular Meeting, March 15, 1933

OLIVER S. ORMSBY, M.D., *President, Presiding*

LICHEN PLANUS. Presented by DR. MARCUS R. CARO (by invitation).

J. G., a white man, aged 72, presents a generalized eruption of six months' duration. According to the history, which is not satisfactory, lesions appeared first on the back of the neck and rapidly spread to the face and scalp. Itching was severe at first and became worse after irradiation, following which the ears became involved and swollen and the lesions spread to the body. As the itching subsided, the spots became dark. For the past twenty years the patient has been taking large doses of potassium iodide daily each winter as a blood purifier. There is no history of syphilis. The blood count and urinalysis were normal, and the Wassermann reaction of the blood was negative.

Over the lumbar spine and on the flexor surface of the wrists are a few pinhead to slightly larger round, elevated, firm, violaceous-brown papules, some of which are flatter and darker. On the face, scalp, ears, neck, upper part of the chest, axillae, inguinal folds and thighs are many pea-sized, slightly depressed, dark brown macules which, according to the patient, are the end-results of the elevated papules. On the face, scalp, ears, neck and dorsa of the hands are many large comedones which, the patient says, were absent prior to the onset of the eruption. There are no lesions on the genitalia, but there are a few silvery striae on the buccal mucosa.

Histologic examination of a papule taken from the lumbar region showed acanthosis of the epidermis, thickening of the granular layer, an indistinct dermo-epidermal junction and a papillary infiltrate of lymphocytes and large dark chromatophores sharply limited below, all consistent with the diagnosis of lichen planus.

LICHEN PLANUS. Presented by DR. J. H. MITCHELL.

This boy, aged 3½ years, was demonstrated two months ago as having lichen planus. The diagnosis was questioned by some of the members, and the suggestion was made that the condition might be due to a fungus infection. The patient is now demonstrated as presenting typical lichen planus undergoing rapid involution with characteristic brown macular relics following the internal administration of sodium thiosulphate.

DISCUSSION

DR. F. E. SENEAR: I think that the first case was extremely interesting for several reasons: (1) The location of the lichen planus was unusual. Of course, we should expect the involvement of the wrists and the buccal mucosa, but the marked involvement of the neck and face coincides with some of the cases with unusual distribution which we have shown here; I think Howard Fox recently wrote on lichen planus in unusual locations. As I have said before, several years ago we showed a case which was disputed largely because the eruption was almost all about the eyes and ears. (2) This patient had lesions of the spiny type or lichen planus pilaris. (3) The patient had an extensive eruption of comedones. I do

not recall having seen the eruption of comedones as an accompaniment of lichen planus, and I doubt whether any relation exists between the two, but if we accept the history of the lesions on the face as being of the same nature as the others, we have another case of lichen planus with atrophy, the second case of this type which has been shown here recently. Another interesting thing was the pigmentation developing in the tissue. Several years ago we had a patient who had been treated for syphilis when in reality he had lichen planus, and it was a question whether the intense pigmentation that was present was not due to the arsenical therapy.

DR. RUBEN NOMLAND: About four years ago we saw a patient with lichen planus and hyperkeratosis about the hair follicles that was analogous to the first case shown here. We considered it a case of lichen planus pilaris.

DR. MARCUS R. CARO: The history is rather vague. The patient stated that he had not noticed any comedones prior to the onset of the eruption, but even now he did not know that he had them until they were expressed. As to the pigmentation, it could not be due to medication because, except for potassium iodide, there was no ingestion of drugs.

CUTIS VERTICIS GYRATA AND ACROMEGALY. Presented by DR. E. A. OLIVER.

S. K., a white man, aged 48, was admitted to the United States Veterans' Hospital on Feb. 3, 1933, for the treatment of acromegaly. He stated that for the past ten to fifteen years he had noticed a gradual enlargement of the extremities and of the facies. At the same time he had observed the appearance of large wrinkles or furrows on the forehead and scalp and a thickening of the lips and eyelids.

Examination revealed the clinical characteristics of acromegaly. In addition, the patient presented a markedly furrowed skin over the scalp and on the regions of the neck and forehead. The furrows were so numerous and deep that they resembled the sulci of the brain. The skin was freely movable over the underlying tissue, and it hung in folds over the occipital region.

Roentgenographic examination of the skull revealed the sella turcica to be of normal size, shape and depth. The bones of the skull were thickened.

The Wassermann and the Kahn tests were negative. The basal metabolic rates were found to be: + 46.8 per cent, + 48.6 per cent, + 53.1 per cent and + 43.1 per cent.

The patient is married and has five normal, apparently healthy children.

DISCUSSION

DR. F. E. SENEAR: Dr. Alderson's recent report of cutis verticis gyrata following an inflammatory condition discussed the infective character of this disorder but did not mention the endocrine factor. We demonstrated at the school the patient shown by Dr. Foerster and Dr. Wieder about two years ago, and one of the men called our attention to the fact that Cushing's textbook discussed a case closely resembling the condition of that patient, and that the association of acromegaly and cutis verticis gyrata had been recognized by him for some years.

DR. RUBEN NOMLAND: In the bulletin of the French Society there is a recent report of three cases of cutis verticis gyrata and acromegaly (Adrian, Charles: Sur la morphogenèse de la pachydermie occipitale vorticillée ["cutis verticis gyrata," cuir chevelu encéphaloïde]: Ses rapports avec l'acromégalie, *Bull. Soc. franç. de dermat. et syph.* [Réunion dermat., Strasbourg] **39**:1485 [Dec.] 1932).

DR. E. A. OLIVER: I have been much interested in this disorder since I reported a case in the ARCHIVES in July, 1922. At that time Alderson reported 2 cases before the American Dermatological Association. Prior to that only 1 case, one by Wise and Levin, had been reported in the American literature.

The first case was described by Jadassohn in 1906. Since that time approximately 150 cases have been reported, so it is not a rare condition.

There has been a great diversity of opinion regarding the etiology of this disease. Many cases have been thought to be due to preceding inflammatory diseases; some cases undoubtedly consist of nevi. Some are due to congenital hypertrophies of the connective tissue of the scalp, while a fourth group consists of changes in the scalp, produced by such diseases as acromegaly, myxedema and leukemia.

This case is similar in many ways to the case shown before this society by Dr. Wieder, and undoubtedly it belongs in the group of cases in which proliferation of the tissues of the scalp has occurred in association with acromegaly.

According to Fischer's classification, this condition should be regarded as "an acute inflammatory condition of the scalp in the form of cutis verticis gyrata" rather than as a true cutis verticis gyrata. True cutis verticis gyrata, according to Fischer, is a congenital anomaly and represents a reversion to a lower form of life.

LICHEN OBTUSUS CORNEUS. Presented by DR. E. A. OLIVER and DR. RUBEN NOMLAND.

A man, aged 47, has an itching disorder of the legs of about four years' duration. Each lesion started as a "pimple" which itched intensely and slowly enlarged. Previously lesions had appeared on the back of the neck.

Indiscriminately scattered over the front and calves of both legs are several dozen lesions, all of which are essentially identical. Each lesion is round or oval and about 1.5 cm. in its largest diameter. They are definitely elevated above the surface and quite sharply bordered. Most of them are dry and slightly scaling, but many present a moist, eroded surface. On the back of the neck and extending into the scalp are many indistinct excoriated lesions.

A lesion on the leg was removed for microscopic examination.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: I am not sure whether this is a case of prurigo nodularis. It seems to me that there is a possibility. In the first place, the patient has areas of dermatitis in several places; he has the area on the neck, and I think it quite possible that he has had lesions or infection on the legs. The lesions are verrucous on top and are not so much covered with epidermis as lesions of prurigo nodularis are as a rule. I think that it is a case of vegetating dermatitis, a dermatitis from pus infection that produces vegetations. Perhaps I am more inclined to make that diagnosis today because we have at the office a boy who two weeks ago had a frank, dirty dermatitis and who now has dirty vegetating lesions on the face and scalp which are not unlike the ones in this case. I think that it is a vegetating dermatitis resulting from an indolent infection.

DR. M. H. EBERT: In this instance the title of lichen obtusus corneus is intended to be synonymous with prurigo nodularis. I noticed one anomalous fact, namely, the presence of areas of lichenification between the nodules. This does not occur in prurigo nodularis.

DR. OLIVER S. ORMSBY: On account of the work of Pautrier on lichenification, and particularly because he included prurigo nodularis in this group, I have been interested in this subject. The disorder that was originally described by Brocq as lichen obtusus corneus was first described in this country by White under the title used by Brocq. Several years previously, Hardaway described the case of a patient who had multiple tumors of the skin with itching, and later Schamberg and Hirschler described a similar condition occurring in the Negro race. Still later, Hyde recorded the case of a patient with lesions which he considered identical with the cases discussed by Hardaway and Schamberg and Hirschler, under the title of prurigo nodularis. Shortly afterward, Zeisler also recorded a similar case under the title given by Hyde and included, among other diseases, lichen obtusus corneus in the group.

Subsequent observations point to a probability that lichen obtusus corneus and prurigo nodularis are identical conditions. In this condition the lesions are rather large, warty or keratotic, discrete, intensely itchy nodules situated chiefly on the extremities. The lesions are persistent; they rarely, if ever, disappear. In a number of instances a new lesion has developed in the area from which one has been removed for a microscopic examination. The skin between the nodules is normal, and the itching apparently is limited to the lesions. These points make it difficult to consider the condition as merely a secondary lichenification.

In his enlarged conception of lichenification Pautrier includes prurigo nodularis as the nodular form of lichenification. In addition, he describes two other forms, a verrucous and a giant lichenification. In the group of verrucous lichenification he includes lichen corneus hypertrophicus (lichen planus hypertrophicus). In the examination of seventeen cases of this type, he found less than half with associated lichen planus lesions or lichen planus histology.

Under the term giant lichenification, Pautrier includes those cases which present plaques and tumor-like lesions associated with itching, crusting and, often, vesiculation, together with patches of mosaic lichenification usually situated in the genital region. Occasionally mycosis fungoides or syphilis is simulated. The plaques are essentially hypertrophic lesions following an itching dermatosis. The histology in the cases he describes was similar to that found in verrucous lichenification not associated with lichen planus.

In conclusion, the identity of prurigo nodularis and lichen obtusus corneus seems confirmed, but these conditions are not related to a variant of lichen planus. The condition appears to be a disease sui generis, and it seems to have a pathogenesis deeper than trauma.

DR. WILLIAM ALLEN PUSEY: I believe there is no reason for confusing hypertrophic lichen planus with prurigo nodularis. I think that in this patient a secondary lichenification may account for the nodularis. The lesions were confined to the legs; they were quite large inflammatory lesions with a raw surface on top, and the case did not coincide with my conception of prurigo nodularis.

PRURIGO NODULARIS. Presented by DR. RUBEN NOMLAND and DR. RALPH SCULL.

A Negro, aged 63, states that his cutaneous disorder began two years ago as a nodulopapular eruption, accompanied by pruritus. It progressed insidiously and involved the upper and lower extremities. The color of the lesions was not noted. He was first seen by us in July, 1932; since then there has been very little change in the condition.

The eruption is limited to the extremities. The lesions consist of hard, conical nodules which vary from 1 to 2 cm. in diameter. The lesions are discrete and occasionally excoriated.

Examination of the blood and urine gave negative results.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: This case resembled prurigo nodularis and is a good illustration of that disease as a contrast to the previous case.

DERMATITIS HERPETIFORMIS (TREATED WITH HEAT THERAPY). Presented by DR. CLEVELAND J. WHITE and DR. JOHN S. COULTER.

A Mexican, aged 48, has a grouped, symmetrical, papular and papulovesicular eruption of about two years' duration. When first seen at Dr. Stillians' clinic about a year ago, the usual therapy, consisting of roentgenotherapy, treatment with arsenic and other treatment, was instituted. No improvement was evident after six months' treatment, and, as the pruritus had become almost intolerable, the patient was given six successive weekly hyperpyrexia treatments with Dr. Coulter's apparatus. This apparatus consists of sixteen 60 watt electric lights. The patient's temperature was raised to 104 F. and kept at that level for four hours. Improvement was indicated after the second treatment and has continued for three months.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: How was the treatment carried out?

DR. CLEVELAND J. WHITE: Dr. Coulter has a closed framework containing sixteen lights, and the temperature can be lowered at any time by shutting off lights. This patient's temperature was raised to 104 F., and was maintained at that level for four hours. The treatment was continued over a period of six weeks, with one treatment a week. The patient felt a little weak after the first treatment, but the results were so strikingly evident that he was satisfied to continue. Before we started the treatment he appeared completely tired out all the time, but after the second treatment with light rays he began to improve markedly.

DR. J. H. MITCHELL: I should like to ask whether this might not be merely a remission. The man still has grouped lesions that appear active to me, and I wonder whether the improvement can be ascribed to the treatment.

DR. L. F. WEBER: This morning we saw a patient with dermatitis herpetiformis who ten days ago had an acute attack. I gave him one injection of a bismuth preparation, and the eruption has cleared up markedly. One might think that medication with bismuth would cure him, but he will probably have another attack in a few weeks.

DR. WILLIAM ALLEN PUSEY: The condition appears to present a picture typical of dermatitis herpetiformis now. Any treatment that will give relief in this condition is worth discussing.

DR. THEODORE CORNBLEET: I have been studying the blood chemistry of patients while they were undergoing heat therapy. We have a sweat bath in which we place these patients, perhaps somewhat similar to the one described by Dr. White. I have noticed that there is a marked change in the blood chemistry of patients subjected to that treatment. Subjectively they feel much better. One striking thing we have noticed is that in chronic urticaria the itching decreases, and I wonder whether Dr. White's case is a coincidence, whether my cases present near coincidences or whether it is possible to change the fundamental chemistry of the skin so as to reduce the pruritus element.

DR. WILLIAM ALLEN PUSEY: Was the patient constantly in a heavy sweat, in spite of the fact that his temperature was 104 F.?

DR. CLEVELAND J. WHITE: Yes, for four hours the temperature was kept at 104 F. This patient was presented to show what happened with hyperpyrexia treatments in one case. The patient did not improve under other methods, but he did improve greatly under heat therapy. There are still a few areas of mild active eruption.

TELANGIECTASIA DUE TO ROENTGEN THERAPY, FIBROSIS OF THE CHEST AND POSSIBLE MALIGNANCY OF THE RIGHT MAMMARY GLAND. Presented by DR. J. H. MITCHELL.

A woman, aged 37, was treated ten years ago for hyperthyroidism. No change in the skin occurred over the region of the thyroid, but within three or four years fibrosis and telangiectasia developed over the right side of the chest. There has been no increase in the size of the area, but there has been a steady increase in the fibrosis of the mammary gland. Recently the patient has been told that she has a sarcoma of the gland, and that immediate amputation is indicated.

The area extends from the base of the neck to and including the upper quadrant of the right mammary gland, and from the left margin of the sternum nearly to the anterior border of the right axilla. In the upper quadrant of the breast there is a dense hard mass of fibrosis which extends beyond the line of telangiectasia but which has the same contour. Characteristic telangiectasia is present throughout the area. During the past two years the patient has been treated by her physician from time to time with carbon dioxide snow, and she is of the opinion that this snow treatment has caused the condition in the breast.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: I have never seen a mass of that thickness and size under a scar following roentgen therapy, though I have seen a great many scars in approximately that location, many of them following treatment of the thyroid. I cannot be satisfied with a belief that this is a fibrous mass; the whole feel of it and the outline make me think that it is a massive carcinoma. It has the feel of carcinoma. I should be surprised if an incision of the lesion does not reveal carcinoma. I am at a loss to know how to connect that mass with a scar following roentgen therapy, and I am also at a loss to call it a simple primary carcinoma beginning in the breast. It has started higher than where carcinomas usually appear, and it extends beyond the breast tissue.

DR. OLIVER S. ORMSBY: The history is interesting. The roentgen therapy was given about five years ago, and the telangiectasia appeared some time later and has gradually increased up to the present time. Like Dr. Pusey, I have not seen a similar case. I have repeatedly seen scleroderma-like thickening, but never to the amount or depth that is present in this case. It is possible that the looseness of the tissue about the breast is a factor in the development of this unusual fibrosis. In view of the slow development of the process and its connection with the scar, the prognosis of its being a benign fibrosis rather than a malignant growth is favorable.

DR. J. H. MITCHELL: I should like to have the opinions of some of the members, for the situation is rather difficult for all concerned. The patient had no treatment except carbon dioxide snow therapy. She is inclined to charge the physician with having produced this lesion with the carbon dioxide snow.

DR. WILLIAM ALLEN PUSEY: Is it possible to obtain a piece of the tissue?

DR. J. H. MITCHELL: I think that amputation is going to be performed soon. I saw the patient only once before. I suppose the growth could be a result of roentgen therapy, produced by treating the thyroid with the tube too close to the breast, without any protection. The process began less than six years ago. There was a gradual onset, and the fibrosis in the breast is not of as long duration as the other phases of the process. The difficulty is the statement made by a roentgenologist last week that the patient has a malignant sarcoma and that immediate amputation is indicated. The sarcomatous change also is charged to the physician; if we could say that the growth is sarcoma we could exonerate him. I find in damage suits that if the physician has not seen the patient within two years, that automatically releases him by the statute of limitations. However, if he has looked at the lesion or treated it in any way, the statute of limitations runs for two years from that time. He had not treated the patient for four years, but during the last two years he has treated her with carbon dioxide snow from time to time. I should like to know your opinion about a biopsy.

DR. OLIVER S. ORMSBY: I should recommend it. If the growth proves to be sarcomatous or carcinomatous, it could be removed before there is any chance of metastatic involvement.

DR. J. H. MITCHELL: I think that would be best. The patient has no glands in the axilla now. The telangiectasia extends a little to the right, but the irradiation was in this direction. I have a case in a woman who was treated on the abdomen. Both sides were treated; on one side the machine was set for filtration, and the filter was left out. This patient had a much deeper and, I think, a firmer mass than is present in this woman's breast.

NOTE.—Two biopsy specimens were taken with the skin punch. The fibrotic skin was thick and firm. After puncture the breast seemed to be almost hollow, and no tissue could be secured. A section of this skin was entirely free from any suggestion of malignancy. Dr. Selim McArthur then made a long incision, confirming the lack of connection of the breast tissue with the integument. The breast tissue was soft and could be readily scooped out with the gloved fingers. Section of the breast tissue disclosed carcinoma, and the entire breast was amputated.

REPORT ON CASE PREVIOUSLY PRESENTED. Presented by DR. A. W. STILLIANS.

A biopsy specimen removed from a papule on the thumb of the patient with tularemia presented at the January, 1933, meeting was shown.

The epidermis was decidedly acanthotic; the papillary layer was edematous and was infiltrated with round cells and a very few polymorphonuclears. Deeper in the corium was a tuberculoid infiltrate, the center of which was composed of epithelioid cells; the protoplasm was vacuolated and poorly stained. About this central infiltrate was a zone of dense round cell infiltrate. The blood vessels were moderately dilated.

MAX S. WIEN, M.D., *Secretary*

Regular Meeting, April 19, 1933

OLIVER S. ORMSBY, M.D., *President, Presiding*

ALEUKEMIC LYMPHADENOSIS CUTIS. Presented by DR. H. E. MICHELSON.

Mrs. Z., aged 54, whose past history revealed nothing of importance, states that in June, 1931, a rather soft, sharply circumscribed, yellowish plaque developed on the bridge of the nose. Gradually similar areas appeared over the face, so that by January, 1932, she had ten or twelve of these areas, and a few flatter, but similar lesions over the chest.

There are about thirty sharply circumscribed nodes scattered over the forehead, ears and face, with one plaque measuring 2 by 3.5 cm. on the right cheek. The skin over the areas is somewhat edematous, but there is no ulceration or crust formation. The nodes are translucent in appearance, soft to palpation and yellowish pink. The general examination, including careful roentgenographic studies of the chest, revealed no pathologic changes.

Several blood counts have been made, and the leukocyte count varied from 9,300 to 15,300. No immature cells were found, and the diagnosis of leukemia could not be established from the examination of the blood.

The microscopic section shows a practically normal epidermis; there is a narrow free zone immediately under the epidermis, and below this, a marked infiltrate, which is not densely packed, reaches deep into the cutis and is composed of rather large cells with deeply stained nuclei. No other types of cells are seen, and the diagnosis of leukemia cutis is made from the examination of the histologic section.

In view of the normal blood picture, the patient is thought to be in the aleukemic stage.

DISCUSSION

DR. F. E. SENEAR: I believe that this is a very instructive case because with the eruption on the face, as we see it alone, I think the first thought would be that of lupus erythematosus. As we study some of the small lesions, particularly those in the region of the chest and under the diascope, I think we obtain a distinct clue that some other condition is present. Perhaps the association of lesions on the body would at first have led us to think of something other than lupus erythematosus. In view of the biopsy specimen shown today, I think that there is no question as to the diagnosis of leukemia cutis of the aleukemic type.

DR. FRED R. SCHMIDT: Some years ago Dr. Senear and I saw a physician who showed changes of lupus erythematosus of the skin with blood and biopsy findings of leukemia. Five years ago this man had lesions similar to the ones now shown. I saw him a year ago, and he still had the lesions, but there was no apparent extension of the process. Clinically, the diagnosis has remained lupus erythematosus.

DR. O. H. FOERSTER: It seems to me that from the cutaneous aspect alone it would be venturesome to make a diagnosis in this unique case. Erythematous lupus, as Dr. Senear pointed out, is what most of us probably had in mind. In addition, the lesion on the right cheek impressed me as one to be differentiated from the angiolupoid of Pautrier to which I think it bears a close resemblance.

DR. PAUL A. O'LEARY: From the lesions on the face I was more impressed with the possibility of a diagnosis of mycosis fungoides than of lupus erythematosus. The frequency with which the infiltrative plaques may involve the eyelids in the early stage of mycosis fungoides is worthy of comment in view of the fact that this patient presents such a lesion on the left eyelid. I do not believe that any of us, with our limited opportunity for study of this case, can dispute Dr. Michelson's diagnosis, but to me the case presents a commentary on the value of the term lymphoblastoma, and I will hazard the forecast that despite the present pathologic picture the final diagnosis will be Hodgkin's disease.

DR. H. E. MICHELSON: This case has been most difficult to diagnose, and perhaps the final decision has not been reached as yet. I heartily agree with the opinion that on first view lupus erythematosus would seem the most likely diagnosis, but on careful analysis one would note the elevated, yellowish, soft, velvety lesions. There are similar lesions on the trunk. The patient was taking large amounts of a proprietary phenolphthalein laxative, and at first I thought that that had some bearing on the eruption. We also treated her with gold and bismuth preparations for more than a month, with no result. The biopsy, I think, conclusively indicates the diagnosis of lymphadenosis cutis. The blood smear has one or two cells suggestive of leukemia in the field. I think that in the past few years, since we have been discussing the lymphoblastomas as a group, we have been thinking of generalized eruptions, but we must not forget that many bizarre and unique lesions may be the initial ones of leukemia.

A CASE FOR DIAGNOSIS. Presented by DR. J. H. MITCHELL.

A widow, aged 38, in excellent general health, presents cutaneous lesions of four years' duration. On the right mammary gland and extending more than a hand's breadth below are three contiguous areas of lesions with normal skin between. Another area is seen to the left of the sacrum.

When the patient was first seen in November, 1932, she had severe and extensive dermatitis venenata about the entire trunk, due to irritants applied for the treatment of these areas. The dermatitis responded very slowly to soothing applications and to radiotherapy. Repeated exacerbations of the dermatitis occurred; they were thought to be due to rayon and other garments. There have been occasional attacks of folliculitis and patchy dermatitis on various parts of the body. There is no adenopathy.

On April 17, 1933, the blood count was as follows: leukocytes, 9,200; polymorphonuclears, 71 per cent; lymphocytes, 24 per cent; eosinophils, 4 per cent; basophils, 1 per cent, and many platelets.

Biopsy disclosed a dense round cell infiltrate immediately beneath the epidermis and apparently involving the epidermis at some points. The lower margin of the infiltrate was an extremely sharp line. All of the vessels in the corium were surrounded by similar infiltrate. In the section available there was no atrophy of the epidermis.

DISCUSSION

DR. H. R. FOERSTER: I consider this a rather difficult case to discuss. The reticular pigmentation, atrophy and telangiectasia are poikiloderma-like features, as Dr. Mitchell has stated. I believe, however, that poikiloderma atrophicans vasculare is a hazardous diagnosis to make in a process that is so localized, in view of the limited knowledge we have of that disease. The histologic examination does not suggest poikiloderma to me because of the pronounced round cell infiltrate of the papillary layer, with a sharply defined lower margin, as in lichen planus, but the compression of the collagen bundles and the displacement of blood

vessels are features that would fit in with a diagnosis of poikiloderma. This case brings to mind cases shown in the past which presented features of both lichen planus sclerosus et atrophicans and poikiloderma, yet lacked distinctive characteristics of either. If this proves to be poikiloderma, we may consider ourselves fortunate in seeing a case so early in its development.

DR. M. H. EBERT: When I first looked at the case at some distance, the marmoration suggested that it might be the type of pigmentation that follows the application of heat and other local irritants, but on closer investigation I found that most of the pigmentation disappeared under the diascope. I should rather hesitate to make a diagnosis of poikiloderma.

DR. O. H. FOERSTER: I think that a diagnosis of erythrodermia of the large plaque type of Brocq should be considered. The woman has a moderately ichthyotic type of skin, and the scale is exaggerated in consequence. A number of macular lesions are scattered here and there which may have some connection with the large patches on the trunk. I think that this disorder should be given consideration in diagnosis.

DR. CLARK W. FINNERUD: I saw only the section and I merely wish to remark that we have seen cases of what we considered poikiloderma which showed histologically as marked an inflammatory reaction as is present in this one. I do not think that poikiloderma can be ruled out entirely from the sections shown.

DR. J. H. MITCHELL: The case is of four years' duration. The lesions Dr. Finnerud spoke of are small, transient areas of dermatitis; they are of no particular importance according to my observations. I first considered a diagnosis of mycosis fungoides, but the absence of pruritus and the lack of response to radiotherapy caused me to abandon that opinion. The patient had a continuous leukocytosis of about 9,000 and an eosinophilia of 4 per cent. When the first severe dermatitis subsided, I began to think of Brocq's disease but the condition does not seem to be of that character. That disorder shows no sharp cellular infiltrate such as we have here. I shall try to get some more material from different areas for study, as I think it would be advisable to do so.

A CASE FOR DIAGNOSIS (SARCOID?). Presented by DR. MARCUS R. CARO (by invitation).

Mr. F. K., a white man, aged 42, first noticed a reddish discoloration on the chin and lower lip about a year ago. Pruritus was present only at the outset. The patches were pale at times but became definitely worse after perspiring and shaving. The findings of the general examination were negative.

The results of the blood count and urinalysis and the Wassermann test of the blood were also negative.

Examination showed two reddish, fairly well defined, elevated and slightly infiltrated lesions. The one on the chin was round and dollar-sized and was separated by a narrow ridge of normal skin from the upper lesion, which was ovoid and extended to the vermilion border of the lower lip. The lesions were covered by intact skin which showed no scale and no follicular involvement, but in which were present many telangiectatic vessels. Telangiectases were also present on the nose and cheeks.

DISCUSSION

DR. RUBEN NOMLAND: I think that there is some inflammatory element present, and a diagnosis of sarcoid is first in my opinion. We cannot decide more definitely than that without a biopsy.

DR. H. R. FOERSTER: I should like to know more about the lesions this man had on the scalp. There is extensive scarring which I thought might have been caused by lupus erythematosus as the lesion on the chin resembles the telangiectatic type of lupus erythematosus.

DR. MARCUS R. CARO: The patient could not give me much information about the history of the condition on the scalp. When he was about 8 years old,

he had some lesions on the scalp which cleared up at that time and did not recur. He was free from cutaneous lesions until about a year and a half ago, when the condition on the chin appeared. Sarcoid was my first provisional diagnosis, but the patient has shown no improvement following ten weekly doses of one-fourth skin unit of roentgen rays and the administration of a solution of potassium arsenite during the same period of time.

DR. H. E. MICHELSON: I thought of a rhinophymatous type of involvement of the chin. You will recall the case reported recently from Dr. Wile's clinic.

DR. CLARK W. FINNERUD: My impression was that biopsy might decide the question. On looking at the lesion I thought that it might be an unusually deep-seated eruption of the lupus pernio type.

DR. MARCUS R. CARO: I shall attempt to have a biopsy made and shall report later.

SARCOMA, PIGMENTED (NEUROGENIC). Presented by DR. E. P. ZEISLER.

A woman, aged 37, has a hazelnut-sized tumor of the left deltoid region which she says has been present for one year.

The lesion is firm, nodular, partially pigmented and fixed with the epidermis. A similar dark pigmented mole is seen lower down on the upper arm, and several small dark moles have recently appeared on the body.

DISCUSSION

DR. H. E. MICHELSON: This patient presents the often recurring problem: What shall we do with moles? The problem is especially difficult when we are alarmed about their being or becoming malignant. In the case of this particular patient it seems to me that the mole on the arm is already malignant; the tissue is bound down, there is marked infiltration beyong the borders of the mole, and the tissue is very hard. I do not think that the other moles are metastatic. Wide excision with fascial removal and subsequent roentgenotherapy is, I believe, the only hope.

DR. CLARK W. FINNERUD: I presume that this is a lesion of the type Dr. Michelson has described, but to me it would not be surprising if on excision we found it to be a hard fibroma. I have seen one lesion similar to this one in color and size, which dimpled the skin as this one does. I do not know whether it had the little processes radiating from it, but I should not be surprised if this lesion proves to be benign.

DR. E. P. ZEISLER: I recently excised a lesion on the leg that was identical with this one, a brown pigmented lesion, which I thought was a neurofibroma, but the pathologic report showed it to be a sarcoma, and about a month later the patient had a recurrence locally. I do not think that this is the type of lesion we classify as a malignant melanoma; I rather believe that it is a neurogenic sarcoma with pigmentation. These lesions are highly radioresistant, and the only hope is wide excision.

A CASE FOR DIAGNOSIS (SCHAMBERG'S DISEASE?). Presented by DR. F. E. SENEAR and DR. MARCUS R. CARO.

B. McC., a white girl, aged 14, had scarlet fever about ten months ago. Soon after the desquamation ceased, a generalized eruption similar to the present one developed, which at that time involved also the face, and which disappeared spontaneously in about two weeks. Four months ago the present eruption was first noticed on the left leg, and it gradually spread to involve both the lower and the upper extremities. There has never been any pruritus or other subjective symptoms. During the month since the patient first came under observation there has been definite fading of the lesions.

The eruption consists of circinate patches varying in size from that of a pea to that of a palm on the anterior surface of the legs, on the thighs, buttocks and sacral region and on the extensor surface of the forearms. In each patch there is a definite but irregular reddish border which contains fine telangiectases and purpuric macules varying in size from that of a pinpoint to that of a pinhead, while the center shows clearing but no atrophy.

Biopsy revealed a thin non-nucleated scale, a moderate degree of acanthosis and slight intracellular edema of the epidermis, a discontinuous granular layer and an intact basal layer. The corium was edematous and showed dilatation of the superficial blood vessels and perivascular edematous mantles of round cell infiltration, with slight hemorrhage. The sweat glands and the deeper part of the corium were normal. No hemosiderin granules were found. The histologic changes lacked the pigment granules of Schamberg's disease and the marked epidermal changes of purpura annularis telangiectodes; they lacked the typical endarteritis and changes in the sweat glands and deep vessels.

DISCUSSION

DR. H. E. MICHELSON: I think that this eruption closely resembles the one that Dr. Zeisler showed recently, and also two cases of my own which had similar eruptions. I think I mentioned that Gougerot had reported a condition which was similar to Schamberg's disease, only it was made up of minute papules, and there was a general distribution. He called the condition purpuric pigmentary lichenoid dermatitis. Until further studies are made and Gougerot's report is evaluated, I feel quite satisfied with the term, for I cannot conceive of Schamberg's disease in the sense of a generalized eruption.

DR. E. P. ZEISLER: Dr. Michelson was so kind as to send me a translation of Gougerot's article, but I must say that the points of differentiation between the two conditions were beyond my comprehension. I should be inclined to classify this case as a generalized or disseminated case of Schamberg's disease.

DR. J. H. MITCHELL: In connection with this case I should like to ask if any one has seen pityriasis rosea with purpuric lesions persisting after involution of the original lesion. During the winter I had a patient who had pityriasis rosea with lesions that remained purpuric long after the pityriasis rosea cleared up. It occurred to me that if such a thing could take place in a definite case of pityriasis rosea under close observation, perhaps it was possible for this case to have begun in that way.

DR. MARCUS R. CARO: It is difficult to fit this case into any of the three conditions ordinarily considered because it lacks some of the findings characteristic of each of them. The picture resembled purpura annularis telangiectodes, but there was not the deep infiltration, and the changes in the sweat glands were also absent.

POIKILODERMA ATROPHICANS VASCULARE. Presented by DR. MINNIE O. PERLSTEIN (by invitation).

Mrs. L. S., a Jewess, aged 45, presents a slowly progressive eruption of about six years' duration, which is entirely asymptomatic.

The eruption consists of generalized, roughly symmetrical, round plaques, varying in size from that of a palm to that of a plate, which involve the entire trunk and the buttocks, thighs and arms, with smaller scattered lesions on the forearms; during the past two months the face has become involved. The involved areas consist of reticular atrophy and telangiectasia and resemble radiodermatitis. The color varies from red to violet and brown. Moderate scaling is present. On two occasions during the past two months vesicles have been observed on some of the lesions. Very little treatment has been administered.

The patient's general condition has been unusually good. At the present time she is in the menopause, with occasional flushing, headache and nervousness, and during the past month she has complained of pains in various muscles of the arms and legs. Physical examination gave essentially negative findings.

Blood counts, serologic examinations and the blood chemistry were negative, and the basal metabolic tests were within normal limits.

A biopsy specimen, taken from an infiltrated lesion on the back, showed atrophy of the epidermis and slight edema. The upper part of the corium was edematous and showed loose mantles of round cells about the vessels, with occasional chromatophores in the papillary layer. The collagen fibers stained poorly in the upper part, and the elastic fibers were fragmented.

In an atrophic lesion similar but more pronounced changes were seen. The basal layer was broken in places by the infiltrate, and the elastic fibers were almost entirely absent in parts of the papillary layer.

DISCUSSION

DR. O. H. FOERSTER: At first glance I thought that the condition resembled about as closely as possible the typical cases of poikiloderma atrophicans vasculare that have been described thus far in the literature. After as close an examination of the cutaneous lesions as was possible in a short time, I concluded that a diagnosis of poikiloderma should be made with reservations. This decision I base particularly on the arcual character of the superficial infiltrates on the back and on the arm, which are of the type that one associates with mycosis fungoides. I regard this disorder as one that frequently simulates other conditions at some time in its course. Although I think many of the features of poikiloderma are present in this case, I hesitate to put that down as a final diagnosis.

DR. M. H. EBERT: I believe that Dr. Foerster's observation in regard to the presence of the infiltrate on the back is pertinent. A case of Dr. Ormsby's that has been under observation for some time in the office closely resembles the case shown, but the majority of the lesions are of the large infiltrative variety suggesting mycosis fungoides with the arciform arrangement and with the other features, including the pruritus. I think that mycosis fungoides should be borne in mind in this case, although the histology was not typical of that disorder.

DR. F. E. SENEAR: I believe, as Dr. Foerster does, that if we take certain of the lesions, particularly the original lesion and isolate them, the condition certainly resembles poikiloderma atrophicans vasculare. The other changes, however, which apparently precede that, when seen alone, make one think of mycosis fungoides. The patient had on one side of the abdominal wall a lesion with a clearing in the center that was distinctly whiter than the rest. The patient recently shown by Dr. Oliver had a clearing in the center of the lesion with a vegetating growth about it. It seems to me that since the first case of poikiloderma was shown here, I think by Dr. Zeisler, all we have seen have been poikiloderma-like changes in association with other disorders. This patient had, as Dr. O'Leary suggested when examining her, an idiopathic atrophy. Whether the atrophic areas are all associated with these scaling patches or not I cannot say. Since we have seen so many poikiloderma-like lesions resulting from preceding inflammatory eruptions, I begin to feel uncertain as to poikiloderma as an entity.

DR. PAUL A. O'LEARY: I have the same concept of poikiloderma as that expressed by Dr. Senear. To me it is analogous to hepatic cirrhosis, which is the end-result of the effect of a variety of agents damaging to the liver. The cutaneous picture we call poikiloderma might well be the end-result of repeated insults from various factors, some of which may be infectious agents. The possibility of mycosis fungoides must also be borne in mind in this case, particularly because of the infiltrated plaques which are present. A year ago Dr. Otto Foerster called the attention of this Society to the association of poikiloderma and mycosis fungoides when he discussed a case of poikiloderma which Dr. Montgomery and I presented here.

DR. FRED R. SCHMIDT: To substantiate what has been said, I wish to refer to the infiltration under the skin. In Vienna I saw a case reported by Fuhe of dermatomyositis in which the infiltrations under the skin were similar to the case

now discussed. I remember that at the time he said that these poikiloderma-like lesions of the skin are merely lesions that one sees in connection with other processes going on under the skin.

DR. O. H. FOERSTER: The pains in the muscles and joints mentioned by Dr. Perlstein should be particularly borne in mind. They are probably also part of the picture.

DR. OLIVER S. ORMSBY: In the early history of poikiloderma, Civatte reported a group of cases which later were entirely isolated from the Jacoby type, so the disease is being restricted. Furthermore, Civatte's poikiloderma has been recently declared by Civatte himself to be identical with Riehl's melanosis, as described during the World War, so it is not a new entity. The theory of an endocrine cause of Civatte's poikiloderma therefore is eliminated as a factor in poikiloderma as now recognized. I think that Dr. Schmidt's remarks are of value because those cases of infiltration must be considered. The concensus appears to be that the Jacoby type of poikiloderma is an entity, but many have expressed an opposite view. As Dr. O'Leary and Dr. Finnerud stated, the poikiloderma syndrome may occur as the result of several diseases. The case before us more nearly corresponds to the original case of poikiloderma atrophicans vasculare of Jacoby than any previously exhibited here. Notwithstanding this, the discussion today demonstrates the difficulty in classifying this disorder.

ANAL DERMATITIS DUE TO THE RESORCINOL IN ANUSOL SUPPOSITORIES: TWO CASES OF POSITIVE PATCH TESTS WITH ANUSOL SUPPOSITORIES AND WITH RESORCINOL. Presented by DR. J. H. MITCHELL.

CASE 1.—A mild hemorrhoid developed in a physician in September, 1932. There was an ample accumulation of anusol samples in his office; for three days he used them as directed. At the end of that time the itching and burning were intolerable, but the hemorrhoid remained. The suppositories were discontinued, and the discomfort gradually disappeared in the course of two weeks. There has been no recurrence.

A patch test on the arm resulted in a severe reaction. According to the information in the hands of Dr. John J. Gill of the Committee on Pharmacy of the Chicago Medical Society, anusol suppositories contain resorcinol (*meta*-dihydroxybenzene). A letter to the manufacturer elicited no reply on this point. As a medical student the patient discovered that a marked sensitization existed as a result of the application of resorcinol to the scalp. A patch test with hydroquinone (*para*-dihydroxybenzene) gave an equally sharp reaction. A patch test with hexylresorcinol gave a very slight reaction. Euresol (mono-acetic acid ester) had been used on the scalp but after a few days a mild dermatitis resulted. A pyrocatechin (*ortho*-dioxybenzene) patch was positive, but less so than with hydroquinone.

CASE 2.—A man, a cosmetic manufacturer, was first seen in January, 1927, with a severe dermatitis about the anal region. He had consulted his family physician for a hemorrhoid. There had been no itching. He was referred to a dermatologist, who instructed him to break an anusol suppository into two parts, one of which was to be inserted and the other to be rubbed about the anal region. A severe pruritus developed. He deserted the dermatologist and consulted a proctologist, who discontinued the suppositories but added other irritants. At the height of the dermatitis the patient was seen by Dr. Mitchell. A treatment for dermatitis was obvious but sensitization to the resorcinol in anusol suppositories was not suspected. The patient was given radiotherapy and soothing applications, with complete recovery.

In April, 1927, the patient was again seen with a mild dermatitis as a result of the appearance of a hemorrhoid and of the use of anusol suppositories. The suppositories were still not incriminated, but they were discontinued. The patient was not seen again until April 1, 1933, when he appeared with an area of dermatitis the size of his palm about the anal region. He stated that another hemorrhoid had

developed and he had applied and inserted the anusol suppository as directed by the dermatologist in 1927. A patch test with anusol suppository gave a violent reaction. A patch test with resorcinol gave a similar reaction. The anal dermatitis subsided with soothing applications and discontinuance of the suppositories.

DISCUSSION

DR. L. F. WEBER: I have had occasion to see several patients who have been treated by anal specialists. I think that we should keep in mind that many ingredients in suppositories can produce irritation; even such a simple thing as cocoa butter may at times cause dermatitis.

DR. M. E. OBERMAYER: I think that we have here a beautiful example of group reaction, since the chemical composition of the substances is so closely allied. We are particularly interested because we are working on crude coal tar, and all these substances are constituents of crude coal tar. I think that resorcinol is a frequent source of irritation.

DR. J. H. MITCHELL: An interesting feature of this case is that Urbach, Nathan and Stern do not agree. Urbach found in 1925 that the two patients sensitized to resorcinol would react to the two isomers of resorcinol. Nathan and Stern found that their patient did not react to the isomers but did react to some of the resorcinol derivatives. We know that in some persons quinine sulphate will cause an eruption, whereas quinidine will not. Urbach gave resorcinol internally and set up a severe generalized eruption. He claims to have desensitized a patient by oral administration of the drug. I should like to give these patients some resorcinol internally, but I am afraid of a too violent reaction.

NOTE.—The patient was later tested with hydroquinone and pyrocatechin and gave sharp reaction to both isomers.

NEW YORK DERMATOLOGICAL SOCIETY

EDWARD R. MALONEY, M.D., *Secretary*

Regular Meeting, April 25, 1933

GEORGE M. MACKEE, M.D., *President*

SUBCUTANEOUS FAT NECROSIS OF THE NEW-BORN. Presented by DR. HOWARD FOX.

Baby B., the son of American parents, is the first child of his mother, aged 34. Labor lasted five days, and forceps were used in the delivery. At the age of 2 weeks, the baby was taken to the New York Nursery and Child's Hospital for the treatment of convulsions, at which time the eruption was noticed by the hospital physicians. It consists of subcutaneous nodules the size of a chestnut in each cheek and several smaller ones at the side of the neck. The nodules are covered by normal skin, and are hard to the touch and freely movable on the deeper parts. The convulsions soon subsided and did not recur. The baby weighed 7 pounds and 11 ounces (3,512 Gm.) at birth, and now weighs 8 pounds and 8 ounces (3,827 Gm.). At no time has there been a rise in temperature or a gastrointestinal disturbance. Microscopic slides showing the usual picture are presented.

DISCUSSION

DR. J. F. FRASER: The histologic picture is that of a foreign body granuloma in the subcutaneous fat. It is not that of true fat necrosis.

DR. W. J. HIGHMAN: There are certain changes taking place in the fat. The term "obstetric lipophagic granuloma" seems to be a better designation.

DR. F. C. COMBES: I wonder how much the trauma at delivery has to do with the disease.

DR. HOWARD FOX: This is the seventh case of the disease that I have seen in a comparatively short time and the fourth that has been histologically proved. All of the cases have many striking similarities. They represent a benign condition which may be localized or cover fairly extensive areas. The indurations are invariably insensitive and hard, and disappear spontaneously in a few weeks or months. The babies are often large and are often born after difficult labor. I agree that the term "obstetric lipophagic granuloma" is better than "subcutaneous fat necrosis," as the granulomatous infiltration with foreign body giant cells is always a striking feature.

LINEAR SCLERODERMA. Presented by DR. HANS J. SCHWARTZ.

This girl, aged 9 years, was previously shown before the society at the November, 1932, meeting, and is again presented to show the improvement of the condition after nineteen weekly injections of 1 cc. of a new pancreas hormone have been made into the buttocks. The induration of the skin in the affected area seems distinctly less, and the skin is softer and more pliable.

A CASE FOR DIAGNOSIS (PIGMENTATION OF THE NECK; NODULAR NEVOID LESIONS OF THE THIGH). Presented by DR. FRED WISE.

A married woman, aged 38, applied for treatment at the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital a few days ago. She shows two different types of cutaneous lesions; the front and sides of the neck exhibit a mottled, dark brown, widespread pigmentation which extends a short distance over the upper portion of the chest. It is said to be of six years' duration and is not the result of sunburn or of locally applied irritants. On the sides of the neck there are several discoid, depigmented, lentil-sized areas, resembling syphilitic leukoderma coli. Itching of moderate degree is present. The history as to ingestion of drugs is negative. A blood test has not been obtained; the history as to syphilis is negative.

On the anterior aspect of the midportion of the right thigh, extending over an area roughly 6 inches (15 cm.) in diameter, is a group of about fifteen nodules; they are dark brown and somewhat violaceous, sharply defined, markedly infiltrated and nonscaly, and they vary in size from that of a pea to that of a hazelnut. There is a remote resemblance to lichen hypertrophicus, but itching is absent, and the patient states that the lesions have been present since childhood. She also complains of frequent attacks of urticaria. Biopsy is refused.

DISCUSSION

DRS. F. C. COMBES and C. M. WILLIAMS: The lesions on the leg are not nevi. The patient's ovaries have been removed, which may be responsible for the pigmentary lesions on the neck.

DR. E. F. TRAUB: I think that the lesions on the neck are similar to those of a patient whom I presented at a previous meeting with poikiloderma of Civatte, a condition which is most common in middle-aged women approaching the menopause.

LICHEN NITIDUS. Presented by DR. FRED WISE.

A girl, aged 19, born in the United States and apparently robust and in good health, from the clinic for diseases of the skin of the New York Post-Graduate Medical School and Hospital, has an eruption of three weeks' duration. It involves the flexor surfaces of the upper extremities and the wrists, and the left shoulder. The lesions consist of rather small, well defined, pinhead-sized, erythematous, raised papules, arranged in groups forming oval and discoid plaques

and situated chiefly on the anterior surface of the wrists and the midportion of the forearms; there is one group on the left shoulder. There is more inflammatory reaction in all of the lesions than is commonly encountered in lichen nitidus; the eruption resembles that of lichen scrofulosorum. The histology, however, is characteristic of lichen nitidus.

A section of tissue is presented for demonstration. A comparison of the section with sections obtained from established cases of lichen nitidus revealed identical changes.

DISCUSSION

DR. W. J. HIGHMAN: Clinically the condition is not lichen nitidus. Under the microscope, however, the lesions look like lichen nitidus; but sometimes what histologically looks like lichen nitidus proves to be one of the tuberculids. The condition seems more like lichen scrofulosorum than any other condition.

DR. HOWARD FOX: The term nitidus, meaning bright and shiny, would not apply to these lesions, which are reddish, scaly and without a shiny appearance. I agree with Dr. Highman that lichen scrofulosorum is a more likely diagnosis, in spite of the fact that the lesions of this disease are more frequently seen on the trunk.

DR. H. H. WHITEHOUSE: I agree with Dr. Highman in favoring lichen scrofulosorum rather than lichen nitidus. The lesions are not so abundant nor the groups so disseminate as in the more classic cases.

DR. E. R. MALONEY: I agree with Dr. Highman that the condition does not look like lichen nitidus clinically, but that the histologic picture closely resembles that of lichen nitidus. I favor the clinical diagnosis of lichen scrofulosorum, even though the lesions in this case are on the arms and not on the trunk.

PEMPHIGUS VULGARIS WITH EXTENSIVE PIGMENTATION IN A NEGRESS. Presented by DR. HOWARD FOX.

A mulattress, aged 48, born in the United States, had always been in robust health until fourteen months ago, when an eruption appeared on the scalp. It then appeared on the elbows, and attained its maximum extent in five months, eventually developing as a symmetrical and profuse eruption of bullae and crusts on the trunk and the extremities. The patient entered Bellevue Hospital four months after the onset and remained there for three months. At the end of that time the bullae and crusts had disappeared, except on the scalp, and a dark brownish pigmentation had appeared. During the first three months of the attack she lost 38 pounds (17.2 Kg.). Three months later, a second generalized attack similar to the first occurred. The active lesions recently healed and again were followed by marked pigmentation. Abraded and crusted lesions, scattered over the scalp, remain. They have never disappeared since the beginning of the illness. On examination, the Nikolsky sign was absent. The urine and the red cell count were normal on frequent occasions, except once, when there was a temporary leukocytosis of 15,000 cells. The Pels-Macht test was positive.

A CASE FOR DIAGNOSIS (LICHEN PLANUS? RADIODERMATITIS? ACRODERMATITIS ATROPHICANS?). Presented by DR. EUGENE TRAUB.

A woman, aged 44, born in the United States, presented an eruption limited to the extremities, of about five years' duration. The skin generally is excessively dry. The eruption is most pronounced over the anterior and the lateral aspects of the lower parts of the legs, where it presents a glazed, violaceous appearance that suggests the confluence of many small, annular lesions. There is some thickening of the skin of the legs; in some areas there seems to be definite atrophy. The eruption is intensely pruritic. On both forearms, over the extensor aspect, there are some lichenification and scaling, suggesting an eczematous process with lichenification—possibly a neurodermite. The patient has been given roentgen treatment

once a week over all the areas for a period of more than four months, with little relief from the itching but with some improvement in the eruption.

A number of diagnoses have been considered, including lichen planus with roentgen sequelae, poikiloderma and scleroderma with roentgen changes. A biopsy has been performed, but the report is not yet available.

DISCUSSION

DR. FRED WISE: I think that the eruption undoubtedly represents the early stages of acrodermatitis chronica atrophicans.

DR. H. J. SCHWARTZ: I agree with Dr. Wise's conception of the case.

DR. H. H. WHITEHOUSE: Acrodermatitis chronica atrophicans would be the most logical diagnosis. It is possible that some of the atrophy and telangiectasia are due to the roentgen rays.

DR. C. M. WILLIAMS: I agree with the diagnosis of acrodermatitis, as stated by Dr. Wise, and should call attention to the atrophy on the knees.

DR. W. J. HIGHMAN: I think that the condition is one of the many disturbances of the capillaries of the skin; one diagnosis to be considered is that mentioned by Dr. Wise. Another that may be considered is poikiloderma. There are telangiectasias and atrophy of the skin. It may be a little early to venture this opinion, but few of us are able to observe conditions of this sort from the beginning and study the developments; but I have no doubt that this eruption belongs to the group of disturbances of the capillaries of the skin, and Dr. Wise's suggestion is as acceptable as any other.

DR. P. E. BECHET: The patient has a punctate atrophy of the knees, suggesting guttate morphea, and some of the patches are circumscribed and hard, suggesting scleroderma and acrodermatitis chronica atrophicans in the same patient. Such cases have been reported by Dr. Wise.

DR. F. C. COMBES: I agree with Dr. Wise and Dr. Williams that the condition is an early case of acrodermatitis chronica atrophicans. Both the infiltrative and the atrophic stages are present. On the left arm an ulnar band of scleroderma is beginning.

DR. E. F. TRAUB: The only reason the possibility of lichen planus was stressed was because of the intense itching accompanying the eruption. I do not believe that this feature is commonly present in acrodermatitis chronica atrophicans or in scleroderma. The location of the lesions is somewhat unusual for acrodermatitis, though it might favor a diagnosis of scleroderma.

LUPUS ERYTHEMATOSUS AND SYPHILIS. Presented by DR. HOWARD FOX.

R. C., aged 58, a painter, contracted syphilis twenty-one years ago. Five years later an eruption appeared which, as presented, covered the entire left cheek. Five years ago (sixteen years after the initial lesion) ulcerating nodules appeared about the lips, chin and legs, which healed and left soft, pliable, punched-out scars, which are grouped to form portions of circles. The scars are unmistakably the result of syphilis. Other scars suggesting a late syphilid are also present on the leg, some of them—according to the patient's statement—having been caused by shrapnel wounds. The eruption on the left side of the face is a superficial, diffuse, dull, reddish area, which is dry, nonitchy and sharply marginated. The border is slightly elevated and is not nodular or beaded at any point. Diascopic pressure failed to show the presence of apple-jelly nodules. In the early stage of the syphilitic infection, treatment was inadequate. Recently the patient has received nine injections of neoarsphenamine and six of bismuth solution, without any appreciable effect on the eruption.

Histologic examination at the border of the patch on the cheek was made by Dr. T. J. Riordan, who reported: There are a thickened, adherent scale which dips into the follicular openings, a loose reticulum with markedly dense infiltration (round cells and plasma cells), swollen blood vessels, destruction of the elastic

tissue fibers and, in places, a tendency to basophil degeneration. The picture is strongly suggestive of lupus erythematous. A diagnosis of syphilis can be considered, but the changes in the blood vessels are not characteristic of the disease.

LUPUS ERYTHEMATOSUS PEMPHIGOIDES. Presented by DR. EDWARD R. MALONEY.

P. J., a white man, aged 36, born in Scotland, presents on the trunk (the back and the chest) and the scalp a profuse eruption of excoriations and crusted lesions, resulting from broken bullae; some unbroken bullae are visible on the forearms. On the middle of the face there are some erythematous and scaly, slightly crusted lesions resembling somewhat the lesions of lupus erythematosus. The eruption started four months ago. The general condition of the patient is good.

DISCUSSION

DR. HOWARD FOX: I think that lupus erythematosus pemphigoides is the probable diagnosis, though it would be necessary to make a microscopic examination to prove it.

DR. FRED WISE: Dr. Goeckerman and Dr. Montgomery occupied themselves with cases of this kind from the histologic standpoint and believe that they are able to differentiate them on histologic grounds. I suggest that Dr. Maloney send a specimen to Dr. Montgomery.

LATE CONGENITAL SYPHILIS WITH EXTENSIVE SCARRING AND EXOPHTHALMOS. Presented by DR. HOWARD FOX.

E. C., a man, aged 25, an Italo-American, was born in the United States. The following history was obtained from the patient's mother, who came to the United States when 15 years old; shortly after this she married. She had a series of six pregnancies resulting in premature births; following these a child was born at full term, who lived three days. The eighth pregnancy resulted in a child who lived ten months. The patient is the ninth child. Four children were subsequently born, one of whom died of influenza. The other three, all of whom were girls, are still living and apparently well. Two are married, one having two children and the other one. All of these daughters and their children are said to be in good health. The father is living (aged 62) and is apparently well.

The patient returned to Italy with his mother when a young child, and at the age of 5 numerous deep sores developed. In a small town, he was seen by numerous family physicians, none of whom benefited him by treatment. He returned to the United States at the age of 18 and was treated in Bellevue Hospital and in the outpatient department, with the result that all of his lesions eventually healed. He now shows numerous deep-seated and deforming scars in the soft tissues overlying the healed depressions in the bony structures. There are about ten separate scars in the frontal and parietal bones, one on the sternum and one below the sternoclavicular joint. The right leg, from the knee to the ankle, shows extensive atrophy of the soft parts and bony deformity, the circumference of the calf being nearly half that of the opposite leg. There are also sharply bordered, soft, pliable scars about the left knee, some of them being connected with bone. There are no active lesions. The Wassermann test was strongly positive. There is a marked bulging of the right eye, with almost complete loss of vision. The details of the ophthalmologic examination will be reported elsewhere. There is a patch of lupus erythematosus on the cheek. Microscopic slides from this patch are presented.

TERTIARY SYPHILIS. Presented by DR. FRED WISE.

A man, aged 47, married, born in the United States, applied for treatment at the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital about three weeks ago. He exhibits a large lesion of the front and

sides of the face, which is most pronounced and active about the lips and chin and which is causing partial stenosis of the mouth. The cheeks show old conspicuous scars with punched-out and gyrate borders and atrophic sunken surfaces. Adjacent to the scars, the skin presents an infiltrated, reddened, somewhat scaly, diffuse inflammation, resembling the flat variety of lupus vulgaris but exhibiting no signs of apple-jelly nodules. A few scattered, infiltrated, flat, erythematous plaques are noticeable on the cheeks below the area of scar tissue. One of these active areas was removed for histologic examination. The alae nasi were destroyed by an ulcerative process which extended for a short distance into the nares. The bulb of the nose was not attacked by the disease. On the right side of the nose, near the ala, is a small, deep ulcer which extends partly to the adjacent cheek; and the lower lip on the left side also exhibits a small ulcer. The entire process is most pronounced circumorally, and is said to be of five years' duration. The patient stated that five years previously the Wassermann test was negative. The test taken on the day of his first visit proved to be 4 plus. The history as to syphilis was negative, and the patient states that he has never suffered ill health. His wife's blood test is said to be negative. There were no pregnancies.

The histologic report by Dr. Satenstein stated that the tissue showed no changes which could be definitely interpreted as being of either syphilitic or tuberculous nature, but that the finding of a few giant cells deep in the cutis rather favored the diagnosis of lupus vulgaris.

After three intramuscular injections of bismuth, a pronounced improvement in the lesions was obvious.

DISCUSSION

DR. HOWARD FOX: From the clinical standpoint alone, I consider that the condition is a nodular syphilid, as some of the scars have a typical punched-out appearance. I should exclude lupus vulgaris because there is no involvement of the nasal mucosa, in spite of the extent of the eruption, and there is no destruction of the cartilage of the tip of the nose, with the beaklike appearance so characteristic of severe lupus of the nose.

DR. W. J. HIGHMAN: I do not think that this condition is lupus vulgaris. It suggests syphilis; and while it is well known that syphilis and tuberculosis are often difficult to differentiate under the microscope, nevertheless, the appearance of the vessels and the infiltration in this specimen favor syphilis.

A CASE FOR DIAGNOSIS (PITYRIASIS RUBRA PILARIS?). Presented by DR. FRED WISE.

A man, aged 35, born in the United States, first applied for treatment at the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital about three weeks ago. (He was demonstrated on a previous occasion, April 11, 1933, before the Manhattan Dermatological Society by Dr. Max Scheer, as having pityriasis rubra pilaris.)

Histologic examination revealed no evidence of pityriasis rubra pilaris or of psoriasis. In one small area of the section, the epidermis presented a dyskeratotic alteration which Dr. Satenstein believed bears a resemblance to the epidermal changes of Darier's dyskeratosis follicularis vegetans.

SUBSEQUENT NOTE.—Three weeks after presentation, a typical and unmistakable eruption of pityriasis rubra pilaris appeared on the abdomen.

DISCUSSION

DR. HOWARD FOX: I cannot accept the diagnosis of pityriasis rubra pilaris. There are no typical acuminate papules in the vicinity of the eruption, the typical palmar keratosis is absent, and the scalp shows no scaling.

DR. GEORGE M. MACKEE: Histologically, the condition in the slide examined is not pityriasis rubra pilaris, and there is an area that shows dyskeratosis, which one would not expect to find in an eruption of this sort. While the eruption is not

sufficiently follicular for pityriasis rubra pilaris, I should not care to rule out that diagnosis definitely. Arsenical dermatitis might be considered. The margins of the eruption are too sharp and the distribution too symmetrical and peculiar to permit a diagnosis of dermatitis venenata from crude oil products.

DR. W. J. HIGHMAN: The slides do not suggest Darier's disease. There is no dyskeratosis. There is little infiltration, only a certain amount of hyperkeratosis. There happened to be no follicular plugs in the section I saw, and without them I should be inclined to exclude both pityriasis rubra pilaris and Darier's disease. The slide is that of a nondescript dermatitis. The clinical picture alone is that of subacute dermatitis.

DR. J. F. FRASER: There are not sufficient data on which to establish a diagnosis. None of the histologic features of Darier's disease are present.

DR. GEORGE M. MACKEE: Dr. Satenstein made the simple statement that the area of dyskeratosis resembled that seen in the early stage of Darier's disease. There is, of course, no question of Darier's disease in this case, and no diagnosis to that effect was made.

BROMODERMA (NODULAR). Presented by DR. FRED WISE.

A man, aged 25, is presented as having a case of erythema nodosum due to the ingestion of bromide salts. He has taken bromides for three weeks. Nodules varying in size from that of a pea to that of a walnut are present on the upper and lower extremities. They are dusky red, slightly elevated, well defined, smooth, nonscaly lesions which are both painful and tender on pressure.

A CASE FOR DIAGNOSIS. Presented by DR. E. F. TRAUB.

A woman, formerly presented at the March meeting, had peculiar, hard lesions on the cheek resembling calcified milia or keloid. Another section has been removed for examination, and from the cutting it seemed that the cartilage was being encountered. Microscopic examination revealed definitely calcified milia.

MONILIASIS. Presented by DR. EUGENE TRAUB.

A boy, aged 11 years, formerly presented at the March meeting, had a condition in the mouth for eight years. A culture of the stool was made, and from this a yeastlike organism was grown in which, however, typical mycelia failed to develop, even on corn agar. Monilia albicans has been grown from the oral lesions.

MINNESOTA DERMATOLOGICAL SOCIETY

D. D. TURNACLIFF, M.D., *Secretary*

April 5, 1933

E. Z. SHAPIRO, M.D., *President, Presiding*

LUPOID OF BOECK. Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. W., aged 35, is presented because of two indurated plaques on both cheeks. The areas are about the size of a quarter and are adherent to the underlying skin. They have been present for two years. The lesions are not elevated; in fact, a slight depression is noted. The areas are dark blue and have remained unchanged in size for several months. Microscopic sections showed a firmly packed dense infiltrate of epithelioid cells surrounded by a very thin zone of lymphocytes. The Pirquet and Wassermann reactions were negative.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: The patient shows the deep-seated plaques typical of sarcoid of Boeck. The histologic picture, as might be expected, showed lobulated accumulations of epithelioid cells surrounded by a fringe of lymphocytes.

A CASE FOR DIAGNOSIS (NODULAR SYPHILIS? SARCOID?). Presented by DR. H. E. MICHELSON, Minneapolis.

This patient was shown at the last meeting of this Society in Minneapolis, at which time no definite diagnosis was made. Since then she has received six intramuscular injections of mercury salicylates. The lesions have definitely involuted. A second biopsy specimen was shown.

DISCUSSION

DR. PAUL O'LEARY, Rochester: The superficial character of the lesions, the comparative absence of induration, the lack of response to the therapeutic test for syphilis and the nonexistence of scarring in view of the long history are in favor of sarcoid rather than of syphilis. The histologic section gives inconclusive evidence, but the diagnosis of sarcoid seems justifiable.

DR. H. E. MICHELSON, Minneapolis: The patient has been observed for several months but it has been impossible to make a diagnosis. The microscopic picture favors syphilis. The lesions certainly are not characteristic of sarcoid. The serologic reactions have been constantly negative. The lesions receded previously without treatment, and they also partially disappeared recently with antisyphilitic treatment. The diagnostic problem is most difficult.

PAPULAR NECROTIC TUBERCULID. Presented by Dr. H. E. MICHELSON, Minneapolis.

L. P., a girl, aged 18, is presented because of numerous hard papular lesions on the palmar surfaces of the finger-tips and on the backs of the hands. There are a few similar lesions on the legs and the ears. The patient has the chilblain type of circulation, her hands and feet being always cold and clammy. The Pirquet reaction was strongly positive, and the Wassermann reaction was negative. General examination revealed no active tuberculosis. Gold and sodium thiosulphate have been given intravenously, and bismuth intramuscularly. The patient was subjected to a diet high in vitamins, and general ultraviolet irradiation was given. Improvement has been marked, but there has been one relapse. Histologic observations showed the characteristic features of papular necrotic tuberculid.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: The patient's condition has improved remarkably with treatment taken by mouth and with injections of bismuth. I have recently observed that certain forms of tuberculosis of the skin respond to injections of bismuth.

GUMMAS. Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. S., aged 70, is the mother of six children. She has had no miscarriages. The Wassermann reaction was negative on three occasions. The patient is presented because of two large ulcers on the forearm, which are of three years' duration. The condition was diagnosed as sporotrichosis and treatment with potassium iodide was given, without result. Healing is slowly advancing with treatment with bismuth and neoarsphenamine.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: The worst feature of this case is the lack of response to therapy.

DR. JOHN BUTLER, Minneapolis: The lesion on the palm is different from that on the arm; it has a gradually sloping, elevated, papillomatous border. The condition may be blastomycetic dermatitis.

A CASE FOR DIAGNOSIS (ANORECTAL SYPHILOMA OR TUBERCULOSIS COLLIQUATIVA). Presented by DR. H. E. MICHELSON, Minneapolis.

O. J., a man, aged 51, has had draining fistulas around the anus for the past six years. The fistulas were excised surgically in 1929 and in 1931, with recurrence on each occasion. He has inflammatory nodules and five or six draining sinuses involving an area about 10 cm. wide on either side of the anus. Proctoscopic examination showed no involvement of the rectum, although hemorrhoids and an adenoma were found. The Pirquet reaction was 4 plus; the Wassermann reaction was negative eight times. A roentgenogram of the chest gave negative findings for tuberculosis. Biopsy showed a deep-seated infiltrate composed of plasma cells, round cells and giant cells, with definite areas of necrosis and sinus formation.

DISCUSSION

DR. PAUL O'LEARY, Rochester: I have seen several patients with this type of pyodermia of the buttocks. In the majority of instances the involvement has been much more extensive than in this patient, and the duration of the condition has been considerably longer. After several years patients with this condition become debilitated and almost cachectic. In the differential diagnosis, syphilis and tuberculosis as well as pyodermia must be considered. Efforts to prove the existence of tuberculosis in such patients are usually futile, whereas the incidence of syphilis is rather high. In patients in whom serologic reactions have been positive the early therapeutic response to antisyphilitic treatment is rather encouraging, although relapse and extension of the process occur even while the patient is under treatment. It is my concept that lesions of this type frequently start as a syphilitic eruption; a gummatous lesion breaks down and a second infection is engrafted on this, which produces the picture of pyoderma. The combination of surgical excision of the granulomatous indurated areas, allowing the process to granulate, and antisyphilitic treatment has been successful, although it is a long drawn-out procedure. The condition may be classified as a type of pyodermia gangrenosa in which syphilis is one of the etiologic agents.

PORRIGO AMIANTACEA. Presented by DR. S. E. SWEITZER, Minneapolis.

A white woman, aged 40, has lesions on the scalp which have been present for the past three months. There have been no subjective symptoms. She has been unable to clear up the scalp by any amount of shampooing. Examination revealed two plaques on the scalp with an asbestos-like scale extending from the skin up the boles of the hairs.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: When the patient entered the hospital the lesions were more typical of porrigo amiantacea than they now are. Asbestos-like areas extended onto the hair follicles; one was about the size of a quarter, and the other, about the size of a dime. The lesions were hyperkeratotic, and the scale was of asbestos-like consistency. The only article on this disease that I could find in the American literature was one by Becker and Muir (Tinea Amiantacea, ARCH. DERMAT. & SYPH. **20**:45 [July] 1929). They reported three cases of this disease and found a yeast in the scales. The condition is certainly of the same type as that in cases which have been reported in Europe. In some patients the lesions respond rapidly to the administration of ointment of ammoniated mercury.

DR. H. E. MICHELSON, Minneapolis: I think that the name connotes a much graver condition than the disease warrants. There are scars some of which form

collars about the hairs, and I presume that the condition could be called porrigo amiantacea. Dr. Rusten, formerly of the clinic of the University Hospital, took notes on a similar condition which he saw in Vienna, and my impression from his description was that the collars resemble the stems of tiny clay pipes, with the hair coming through the lumen.

LYMPHANGIOMA CIRCUMSCRIPTUM. Presented by DR. S. E. SWEITZER, Minneapolis.

A white woman, aged 58, has lesions about the eyes which she states have been present for the past ten years. They caused no trouble until recently when they began to interfere with reading.

Examination revealed numerous brownish lesions about the eyes; they were soft and emitted a milky fluid when punctured. They varied in size from that of a pinhead to that of a split pea. A diagnosis of lymphangioma circumscriptum was made.

DISCUSSION

DR. JOHN BUTLER, Minneapolis: The condition is cystic whatever the nature of the fluid found. It is not lymphangioma circumscriptum.

DR. JOHN F. MADDEN, St. Paul: I agree with Dr. Butler that the eruption is a degenerative process. The patient also has xanthelasma on the skin of the eyelids, which is another type of degeneration.

DR. H. E. MICHELSON, Minneapolis: I think that this is a unique case. The tiny bladder-like cysts are apparently filled with a clear fluid which may be lymph or, possibly, sweat. I saw a patient in whom there were similar lesions on the shaft of the penis. The cysts were punctured, and the base was then cauterized; there was no recurrence.

DR. JOHN F. MADDEN, St. Paul: There is no definite proof that the fluid is lymph. The lesions may be cystic degenerations of the meibomian or sweat glands, and the fluid may be a mucoid substance. A biopsy specimen should be taken to establish the diagnosis.

MORPHEA. Presented by DR. S. E. SWEITZER, Minneapolis.

A normally developed girl, aged 10, has three firm doughy areas on the right side of the face varying in size from that of a dime to that of a half dollar. The lesions are white and are surrounded by a faint lilac zone. Beneath the jaw on the right side there are a mottled area with increased pigmentation and a peripheral zone of decreased pigmentation.

A biopsy specimen was shown. The child's father stated that the eruption started two years ago as a white spot the size of a dime above the angle of the right mandible. The lesion slowly enlarged until it covered the right check, and two similar lesions appeared, one under and one at the side of the right eye. The lesions have also grown slightly. There has been slight itching but no pain. The past history and the family history are essentially without significance.

DISCUSSION

DR. JOHN F. MADDEN, St. Paul: Some observers associate juvenile cases of morphea or scleroderma with dysfunction of the thyroid gland and determine the basal metabolic rates as a routine procedure. I should like to know whether any one present has been able to demonstrate such an association.

DR. PAUL O'LEARY, Rochester: At the Mayo Clinic we have studied the basal metabolic rates of practically all our patients with morphea and have found them very inconsistent. The great majority are within normal limits, with a few above and below normal. In my experience, the estimation of the basal metabolic rate is of no value in determining the etiology of or the treatment for this disease.

CARCINOMA OF A MALE BREAST. Presented by DR. H. E. MICHELSON, Minneapolis.

J. C., a man, aged 51, has noticed a change in the right nipple for one year. The lesion consists of a fungating mass 3 cm. in diameter, which has replaced the nipple. There is infiltration but no fixation to the wall of the chest. Adenopathy is present in the right axilla. Biopsy showed that the condition was adenocarcinoma.

DISCUSSION

DR. E. Z. SHAPIRO, Duluth: At a recent pathologic conference in Duluth it was pointed out that carcinoma of the male breast is more rapidly fatal than that of the female breast. Deaver has reported approximately 120 cases.

DR. F. R. WRIGHT, Minneapolis: The tumor is a papillary carcinoma of the skin which has developed over the glandular tissue and has extended down into the gland. It is not necessarily very malignant. When such tumors develop in the gland of the male breast, they are exceedingly malignant.

DR. JOHN F. MADDEN, St. Paul: Dr. Stenstrom, of the roentgenologic department of the University of Minnesota, stated that cases of carcinoma of the male breast make up about 1 per cent of all cases of carcinoma of the breast seen at the University Hospital. This is the third patient with this condition that he has seen within the past three years.

DR. F. R. WRIGHT, Minneapolis: I should class the tumor as a carcinoma of the skin over the breast. It is not a carcinoma of the breast, but has spread down into the breast.

DR. S. E. SWEITZER, Minneapolis: I think that when the tumor is sectioned it will be found to be very malignant.

DR. E. Z. SHAPIRO, Duluth: What is to be done? Is a radical resection advisable?

DR. H. E. MICHELSON, Minneapolis: Cancer of the male breast is rare; I think that there have been only three cases at the University Hospital. This patient has an adenocarcinoma, and treatment will be the same as that for cancer of the female breast.

NEVUS PIGMENTOSUS ET PAPILLOMATOSUS WITH UNDERLYING INFLAMMATION. Presented by DR. S. E. SWEITZER, Minneapolis.

A white man, aged 57, has a lesion the size of a quarter in the right inguinal region. It is black and very firm and is raised about 1 cm. above the level of the surrounding skin. It is surrounded by a red areola. There are no palpable glands in the inguinal regions.

The patient stated that the lesion has been present since birth, and that it has been growing rapidly during the past month. On several occasions pus has been squeezed from it. There has been no pain.

It is planned to excise the lesion and to examine it for signs of malignancy.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I think that the lesion is a mole which has become infected. I shall cut it out, section it and see whether or not it is malignant.

DR. H. E. MICHELSON, Minneapolis: There is no doubt but that the lesion belongs to the nevus group, as the patient states that he has had it all his life. There is a question in my mind as to whether it is a benign melanoma. It seems to be above the surface and resembles a keratotic lesion more nearly than it does a mole. A biopsy should be performed.

KRAUROSIS VULVAE. Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. M. L., aged 56, first noticed dyspareunia two years ago, which has become progressively worse. There is atrophy of the external genitalia with whitish plaques and intense pruritus. Biopsy showed the usual findings of kraurosis; there were no signs of lichen planus or of syphilis.

DISCUSSION

DR. PAUL O'LEARY, Rochester: Kraurosis vulvae is a significant entity beacuse of the frequency with which it becomes malignant and because it has always been extremely resistant to treatment. Dr. Counseller and Dr. Learmonth have devised an operation whereby the pudic nerve is severed. It is rather striking to see the rapidity with which the mucous membrane reddens again after the operation. In cases in which leukokeratosis has been present, the plaques have involuted rather quickly. This procedure represents a decided advance in neurosurgery, and I believe that it is of definite value in the treatment of kraurosis vulvae.

NEW ENGLAND DERMATOLOGICAL SOCIETY

WILLIAM P. BOARDMAN, M.D., *Secretary*

Annual Meeting, April 12, 1933

ARTHUR M. GREENWOOD, M.D., *Presiding*

MONILIA INFECTION OF THE MOUTH, FINGERS AND FACE. Presented by DR. JOHN G. DOWNING, Boston.

An American schoolboy, aged 15, from the dermatologic department of the Boston City Hospital, has a condition which started at the age of 5, with sores in the mouth which have been treated at various times. Two years ago the skin at the base of the nail of the right forefinger became painful; one year ago a similar condition arose on the thumbs. He was treated at various hospitals, at which he received intravenous injections of neoarsphenamine and a large number of inhalations of ethyl iodide. About a year ago, lesions appeared on his face; they gradually became worse until he was first seen on May 17, 1932. The lesions at that time resembled an eruption due to an iodide, but with increased hygienic care, a high caloric diet and generalized exposure to sunshine, they disappeared almost entirely, returning later in the fall when he went back to school and was no longer exposed to ultraviolet rays. The lesions became worse until he was hospitalized, in January, 1933. At that time, he showed numerous crusted and hyperkeratotic lesions of from 1 to 2 cm. in diameter, some projecting 1 cm. and simulating cutaneous horns. The entire area of the nose is a crusted, solid mass. The lesions are brownish. The patient shows loss of the nails of the thumb and the index finger. The mouth shows involvement of the tongue and mucous membrane consisting of superficial ulcerations and white deposits.

Organisms recovered from lesions on the face and mouth on several occasions showed by staining (Gram method) single cells, budding forms and thick hyphae.

Cultures on Sabouraud's maltose agar showed an organism which belongs definitely to genus Monilia. The species is not yet definitely assigned but agrees with the cultural characteristics and sugar fermentations of Parasaccharomyces as described by Nye which was found to be identical with Monilia psilosis identified by Ashford. Inoculation into animals further to confirm identity has not as yet been done.

The patient's serum and homologous organism showed 4 plus agglutination at a dilution of 1:320.

Cutaneous tests made with a dilute solution of protein fraction from Monilia obtained from pulmonary mycosis were negative.

Biopsy of the lesion on the face showed marked hyperkeratosis, an occasional area of edema of epidermis, marked growth downward and proliferation of the rete malpighii, large numbers of lymphocytes and plasma cells in the corium and rare foreign body giant cells; there were no organisms demonstrable by the Gram-Weigert stain.

DISCUSSION

DR. JOHN G. DOWNING, Boston: It is my opinion that the condition is merely an infection of the skin and tongue by Monilia.

DR. FRANCIS P. MCCARTHY, Boston: The hyperkeratosis and the acanthosis and cellular reaction of the subcutaneous tissue without the presence of Monilia in the deep tissue are unusual. The cultures are taken from under the crusts, and I am interested in their dependability. The question is whether yeast cells have the property of stimulating the growth of epithelial tissue without appearing in the tissue itself. I should like to hear a discussion as to the action of the various infections due to yeast, and as to whether one often finds the organism in the tissues.

DR. ARTHUR M. GREENWOOD, Boston: In one case which Dr. Rockwood has studied the organism is clearly shown throughout the tissues. The pathologic appearance, however, is not hyperkeratotic, but there is a collection of small abscesses surrounding the organism, and the organism is growing in the tissue.

DR. WALTER T. GARFIELD, Boston: I should like to ask if in the present case the cultures were taken from parts of the body other than the crusts and the scales.

DR. ETHEL MAY ROCKWOOD, Boston: The earlier cultures were taken from the mouth and nails. At that time there was no involvement of the skin. The organism from the mouth and nails was the same as that which Dr. Downing has grown from the skin.

DR. FRANCIS P. MCCARTHY, Boston: I am told that the agglutination of normal serum with this type of organism is much lower than is noted in this case, but I should like to know the real significance of the agglutination.

DR. ARTHUR M. GREENWOOD, Boston: There was no agglutination in the case which my associates and I had.

MELANOTIC SARCOMA. Presented by DR. JOHN G. DOWNING, Boston.

A white American man, aged 38, from the dermatologic department of the Boston City Hospital, presents the following history. One year ago he entered the surgical department because of a painless and noninflammatory growth of one year's duration on the right arm. Biopsy showed melanotic sarcoma. He is now admitted because of pain in the sciatic nerve distribution, which has been apparent for the past three months, and swelling and loss of vision of the right eye for one month.

He shows three small, hard, freely movable masses in the subcutaneous tissues in various places over the abdomen. The nodules have a dark discoloration.

The urine was normal, except for melanin, which was present in large quantities. There was marked secondary anemia. The red blood corpuscles number 2,700,000 and the hemoglobin (Sahli), 58 per cent.

The patient has received symptomatic treatment.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: In connection with this case, I have had some interesting postmortem examinations of melanotic sarcoma in which the primary lesion has been in the eye—a lesion not particularly active—and in which the metastatic tumors appeared later, there having been no suggestion that the eye was involved. May not this so-called primary lesion on the forearm therefore have been a metastatic tumor? The eye is now involved to such an extent that there is marked exophthalmos. May it not be that the lesion of the eye was the primary lesion and that the lesion on the forearm was the first metastasis to be noticed?

GRANULOMA FISSURATUM. Presented by DR. BERNARD APPEL, Boston.

An American housewife, aged 28, from the dermatologic department of the Boston City Hospital, first noticed a slowly growing, relatively asymptomatic lesion in the mouth about six months ago. She wears a loosely fitting upper dental plate. There is a flat, disklike overgrowth of mucous membrane, like a folded coin, at the junction of the right side of the upper jaw and the upper lip.

R. L. Sutton, Jr., first described two cases (ARCH. DERMAT. & SYPH. **26**:425 [Sept.] 1932), and the elder Sutton later published the report of another case (ibid. **26**:865 [Nov.] 1932). The reaction which is often observed following chronic irritation of one sort or another is apparently granulomatous. I think that the lesion is merely an irritation caused by the poorly fitting dental plate.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. RUDOLPH JACOBY, Boston.

A white American housewife, aged 60, was presented to the society in October, 1931, because of an eruption on the face, neck and extensor surfaces of the arms. The diagnosis then made was that of lupus erythematosus disseminatus. Following the advice given at that meeting, the patient was given sixty intramuscular injections of bismuth solution by her local physician. She has also taken some insulin for her appetite. Since she was last presented, the patient has been losing weight and hair, and the lesions have become worse. They are still limited to the exposed areas. The eruption started in May, 1931. The lesions consist of an intense itching erythematous eruption which is said to have started on the face and spread shortly to the arms. The plaques vary in size and shape; most of them are round, with infiltrated margins. Many of them have fused, forming areas 2 or 3 inches (5 or 8 cm.) in diameter. The lesions on the arms are on the extensor surfaces and are violaceous.

Examination of the blood showed a slight anemia of the simple secondary type and slight leukocytosis. The nonprotein nitrogen was 33 mg.; the blood sugar, 98 mg. The white blood cell count was 11,100. A differential blood count showed: neutrophils, 51 per cent; lymphocytes, 39 per cent; endothelial cells, 6 per cent, and eosinophils, 4 per cent. The platelet count was normal.

On seeing the case, Dr. Oliver suggested that brewers' yeast be tried. It was felt that the patients with generalized eruptions should not receive treatment with gold; following administration of brewers' yeast, a remarkable improvement was noticed in a few cases.

DISCUSSION

DR. J. H. SWARTZ, Boston: I should suggest treatment with brewers' yeast. I have seen some of the cases that Dr. Oliver has mentioned, and the results were gratifying. I should also suggest a transfusion. We have given transfusions in two cases, with marked improvement.

PSORIASIS LOCALIZED ON THE FINGERS. Presented by DR. JOHN G. DOWNING, Boston.

A white American man, aged 39, unoccupied since January, 1931, states that an eruption started in 1918 while he was doing general work in the army, part of which had to do with the care of horses. The lesions started on the fingers, which rapidly cracked, and later the scalp, eyelids, ears, nose, knees and elbows became affected. When the patient was first seen, in December, 1930, the skin was normal except for the right elbow and the first, second and third fingers of the hands. The elbow shows typical psoriatic lesions. The fingers, anterior and posterior, are covered with dry, dirty-looking, infiltrated, fissured lesions which on curretting show typical white scaling on bleeding bases. At times around both external auditory meatuses there are redness and scaling.

Repeated cultures and scrapings were negative. The Wassermann test of the blood was negative. General neurologic examination gave negative findings. The patient has atrophic rhinitis.

He has received roentgen therapy, a small amount of arsenic and various ointments. The lesions partly cleared, but recurred. They have never entirely disappeared while the patient has been under observation.

DISCUSSION

DR. BERNARD APPEL, Boston: I agree with the diagnosis of psoriasis, because the patient resembles closely another patient whom I presented during the last year—a young instructor of chemistry who had lesions over the fingers and the hands.

DR. F. S. BURNS, Boston: I could not identify any lesions on the patient's hands which to my mind were consistent with the diagnosis of psoriasis, but I think that he may have had epidermophytosis as well as chronic keratotic lesions. He shows keratosis pilaris on the elbows and knees. On the right side and on the left knee there are many small, individual lesions. The patient may have seborrhea.

DR. JOHN G. DOWNING, Boston: There is no question that this man has had psoriasis on the elbows. He has had at various times definite psoriatic lesions on the ears and on the scalp. It is my opinion that the lesions are definitely psoriatic. I have followed the patient for a long time and see no sign of epidermophytosis. He has had no occupation that might cause hyperkeratotic lesions like these.

NAEVUS FLAMMEUS ET VARICOSUS; HEMIHYPERTROPHY. Presented by DR. JOHN G. DOWNING, Boston.

W. W., a white American electrician, aged 34, states that he has been lopsided since birth. His mother noticed a marked difference between the sides of his body. When he was a boy, the difference was more marked than at present; his face was much larger on the left side, as was the rest of that side of the body, including the arm, hand and leg. He states that he had such a marked limp that his nickname was "Limpy." He also has frequent attacks of hemorrhoids.

He shows a superficial vascular nevus between the eyebrows, about 1 inch (2.5 cm.) square. The left side of the face is still larger than the right. There is a huge superficial vascular nevus on the body extending from the right side of the abdomen, across the chest, to above the left clavicle on to the neck, with an occasional cavernous hemangioma. The left arm is larger than the right by almost 1 inch in circumference. The left hand is much larger than the right. The left leg shows marked varicosities.

The Wassermann reaction was negative.

Roentgen measurements of the bones of the upper extremities and of the feet showed that those on the left are longer than those on the right side from 0.5 to nearly 2 cm.—whereas similar measurements of the bones of the leg and thigh showed that the right were longer than the left by a fraction of a centimeter.

The patient came to my office for inspection of the hand. I obtained a positive fungus growth from the hand and also from the mitten that he wore. The most interesting feature about the condition is the unusual abnormality of the skin, the bone and the soft tissues, and the combination of a vascular nevus on the body with hypertrophy of the soft tissues and enlargement of the bones of the left hand and of the right tibia and varicosities of the leg. This feature has been described in several previous cases. Some have described it as hypertrophy and some as hemihypertrophy. Dr. O'Neil told me of similar cases in which he found a definite arteriovenous aneurysm, and he has consented to say something to us about them.

DISCUSSION

DR. E. E. O'NEIL, Boston: In view of all the work done on this subject in the past few years, I think that it is a fair statement to say that we are forced to the conclusion that these cases of hemihypertrophy associated with increased

growth of the bones of the extremities should all be classified under the large heading of congenital arteriovenous fistulas. I think that we have previously classified them all as separate entities. We know that congenital arteriovenous fistulas show various manifestations such as you have seen in the typical case presented, to wit, increase in the size of the arteries and the veins involved, resulting in varicosities and increase in the width and the length of the bones of the extremities. This is marked in the case presented, the arteriovenous junction descending as far as the bone. This takes place within the bone as well as within the soft tissues, with resulting communications, and the blood passes without benefit to the capillary blood, because of which there is a definite anoxemia with resulting trophic disturbance. The systemic manifestations of this disease are not so manifest as in the acquired type. In the acquired type there is one communication; in the congenital type there are a great many communications. The systemic manifestation is usually cardiac hypertrophy associated with or without bradycardia. The problem is, what to do. First, you make the diagnosis. A glance is usually sufficient, but should there be doubt, a simple tap of the particular vein involved will result in the withdrawal of arterial blood. If that is insufficient, in some of the cases in which the blood may be venous, determination of oxygen may be made. There is an increase in the oxygen content in the blood withdrawn. The treatment, which has been surgical, is almost futile. There are only three cases reported in the literature in which any good has been done at all. Probably the fistulas have been extremely small in these cases. In cases of large arteriovenous fistulas such as this, I doubt whether surgical treatment or any type of treatment is going to be of value. My associates and I, in our work on varicose veins, have seen between fifteen and twenty cases of definitely proved arteriovenous aneurysm in a series of 50,000 varicosities. All of the patients have been admitted to the hospital as having cases of varicose veins. We have attempted as a treatment to sclerose some of the veins in the hope of providing a thrombus which will plug the fistula. We have known of cases in the past in which the arteriovenous fistulas have healed spontaneously. We know further that in four cases dating over four years the injection of a sclerosing solution has brought about at least a temporary cure, and this has been corroborated in other clinics throughout the country.

Dermatologic nomenclature will have to be revised. I think that all these conditions which we have called hemihypertrophy should be classified under the large heading of arteriovenous fistulas, either with or without the superficial manifestations that the condition may cause.

Dr. Morris J. Strauss, New Haven, Conn.: The patient tells me that in the past few years his smaller limb has been growing to the size of the other. Perhaps Dr. Downing can tell whether this is true and, if it is, can explain it.

Dr. E. E. O'Neil, Boston: I measured the legs. The patient feels sure that the involved leg is shorter than what I call the normal leg. As a matter of fact, it is longer. Owing to the tilting of his pelvis, he thinks that it is shorter.

PHILADELPHIA DERMATOLOGICAL SOCIETY

R. L. Gilman, M.D., *Secretary*

April 21, 1933

F. D. Weidman, M.D., *President*

Scleroderma. Presented by Dr. D. M. Pillsbury.

An American girl, aged 5 years, presents a large patch of scleroderma involving the right flank, with extension over the anterior abdominal wall, the right buttock and the right side of the right foot and little toe. The lesions on the trunk and

buttock are of the circumscribed type, and the lesion on the foot is linear. There is marked pigmentation at the periphery of the lesions on the body. The process has been extending for three years.

On examination, the blood count, urine and blood calcium were normal.

DISCUSSION

DR. F. D. WEIDMAN: I thought that the condition was hemiatrophy. The skin is softer over the affected areas and is more pliable than normal skin. The fat is atrophic underneath, the skin is not bound to the underlying parts, and whereas it may be that there is fibrous tissue in the deeper parts to bring it under the category of scleroderma, I think that it would be better to leave out the "derma" in this case. This is a most valuable presentation, because, as we know, in scleroderma there are hemiatrophy and pigmentation in addition. What significance that may have in the way of which of the two came first in the genesis, I do not know. The ribs on the right side appear to me to be much more delicate than those on the left. Roentgen studies of these bones might be made to advantage.

DR. D. M. PILLSBURY: I agree with the suggestion of hemiatrophy as to the lesion on the buttock and that on the trunk. On the foot there were definite sclerodermatous changes in the skin, at least cicatricial changes, because the toe was flexed and somewhat pulled out. We shall have roentgenograms of the ribs taken.

DR. S. S. GREENBAUM: I should like to ask Dr. Pillsbury whether the lesion on the abdomen has received treatment of any sort. It looks like a pigmented nevus the center of which has been treated with roentgen rays or radium.

DR. D. M. PILLSBURY: So far as we know, there has been no treatment with roentgen rays or radium. The patient has received ultraviolet and heat therapy and massage with cocoa butter.

DR. V. C. GARNER: FOX, in the ARCHIVES, has named a modification of the old picture of sclerema atrophy of the subcutaneous fat. I was struck by the soft character of the lesions and by the presence of a distinctly soft velvety feel to the skin, which occurs with atrophy of the subcutaneous tissue.

SCLERODERMA WITH PIGMENTATION; ADDISON'S DISEASE (?). Presented by DR. D. M. PILLSBURY.

An American woman, aged 41, a worker in a tobacco factory, presents generalized pigmentation and patchy sclerodermatous infiltration of the hands, wrists, axillae and trunk. There is marked sclerodactylia. There is some tendency to more marked pigmentation about the mouth, the axillae and the breasts. The buccal mucous membrane shows no pigmentation. There are several areas, particularly over the thighs, which are not pigmented and do not seem to show sclerodermatous infiltration. General physical examination gave essentially negative findings, with the exception of a blood pressure of 100 systolic and 65 diastolic. The Wassermann test was negative. The reaction to the direct van den Bergh test was delayed; the reaction to the indirect test was +0.2 units. The icteric index was 5.

Roentgen examination of the hands showed definite atrophy of the tips of some of the terminal phalanges in a number of fingers of both hands. The entire process is of one year's duration, the scleroderma and pigmentation occurring coincidentally.

DISCUSSION

DR. F. D. WEIDMAN: We all agreed that the condition was extensive bilateral scleroderma. Perhaps the outstanding topic which next merits discussion is whether there is Addison's disease in addition. The papers on scleroderma that came from the Mayo Clinic included this phase, and in them it was the consensus that association with Addison's disease was rare. I suppose that this view must

be accepted; yet in scleroderma we frequently see involvement of the nervous system (often involving the sympathetic system), and we all know what a close anatomicophysiologic (including an embryologic) connection there is between the suprarenal glands and the nervous system. Theoretically, at least, it is not a far stretch of the imagination to see a rôle of the suprarenal glands at least in some cases of scleroderma.

DR. S. S. GREENBAUM: I once had a patient whose condition was exactly like that in the case presented. Pigmentation developed late in the disease; the patient became progressively weakened and died.

DR. A. STRAUSS: Do you think that the woman's occupation would explain the condition? They spray tobacco with arsenic in order to keep out the worms. This may have some bearing on the depigmentation which started after she began to do that work.

DR. D. M. PILLSBURY: Longcope has reported atrophy of one suprarenal gland in a case of this sort. I should like to draw attention to the recent studies of Sellei (*Arch. f. Dermat. u. Syph.* **163**:337, 1931) in which he states that he believes these cases of scleroderma with sclerodactylia belong in a separate group, which he calls "acrosclerosis." In many respects this case fits in with cases he has described, namely, in the extensive bilateral sclerodermatous changes, in the pigmentation, in the vasomotor changes in the extremities, most marked in the feet, and in the general asthenia. Sellei reports that pancreatic extract given by injection or by mouth is very helpful in scleroderma but not in acrosclerosis. Some of his cases have been helped by the Leriche operation.

MULTIPLE NEVI. Presented by DR. H. J. SMITH.

An infant, aged 9 months, presents a growth beneath the left eye which was first noticed two months ago. It was blue, gradually increasing in size and composed of fairly large blood vessels. The child also has a raised, red growth, about the size of a half dollar, on the right arm, just above the wrist; it has been present since birth.

Over the right hip, extending from the symphysis pubis to the vertebral column, is a large pigmented area; portions of the area are covered with hairs, and a small portion is verrucous. This area was noticed at birth; it has remained stationary as to size, but the parents think that it is becoming lighter.

HEMANGIOMA. Presented by DR. D. M. PILLSBURY.

C. M., a white male infant, aged 2 months, presents a large, raised hemangioma involving the left side of the forehead and the upper eyelid.

DISCUSSION ON PAPERS OF SMITH AND PILLSBURY

DR. F. D. WEIDMAN: In Dr. Pillsbury's patient, I could feel two distinct spinal processes on some of the lumbar vertebrae. Roentgenograms of the lumbar spine and the sacrum should be taken to determine the presence or absence of spina bifida, which is known sometimes to accompany congenital defects. I might also state that in cases of very extensive pigmentary nevi, such as appeared in Dr. Smith's patient, there should be an examination of the spinal fluid for melanotic substances. At necropsy in one case I saw the spinal meninges heavily infiltrated with nevus cells; this accounted for the neurologic symptoms which occurred during life.

DR. D. M. PILLSBURY: As I presented the case of hemangioma, I should be grateful for suggestions particularly as to the use of radium about the eye.

DR. J. M. SCHILDKRAUT: I saw a patient with hemangioma of the lid who Dr. Pfahler treated with electrocoagulation and radium, with perfect results.

DR. V. C. GARNER: I saw a child with angioma of the inner aspect of the lower eyelid whose parents wished a consultation with an ophthalmologist. He

advised against radium so near the eye, as he had seen premature cataracts produced by this treatment. Nothing was done in that case, and the angioma has involuted 75 per cent.

DR. S. S. GREENBAUM: Dr. Garner has stated an important point. Children should not be treated until they are a year old, unless the lesions are rapidly growing. At the end of a year the lesions will have stopped growing or will have receded, or they will grow quickly and can then be treated. I believe that electrocoagulation will give as nice a scar as carbon dioxide snow. I believe that the lesion on the eye and the hairy pigmented nevus had better be left alone.

DR. J. M. SCHILDKRAUT: The idea of radium on the lid was to produce a soft scar.

A CASE FOR DIAGNOSIS (TUBERCULOSIS?). Presented by DR. A. D. KING for DR. JOHN H. STOKES.

A colored boy, aged 14, presented the following physical findings in February, 1933: (1) a huge tumor in the left side of the pelvis, apparently arising from the left side of the ilium, associated with other discrete lymphatic enlargements in the left groin, palpable epitrochlears and palpable nodes in the left axilla and cervical region, in the submental region and at the angle of the jaw; (2) bilateral effusion of both knees; (3) bowed tibia, interstitial keratitis and slight edema of the left leg.

Roentgen examination showed changes in the bones which were thought to be secondary to the mass and could be explained as Hodgkin's disease, low grade abscess or, possibly, a primary tumor which had invaded the disk. A roentgenogram showed bilateral effusion of both knee joints. The Wassermann and Kahn tests of the blood were strongly positive. The blood count was essentially normal. Biopsy of the left inguinal gland showed necrotic granulomatous material; smears for acid-fast bacilli and guinea-pig inoculations were negative. A Levaditi stain for spirochetes was also negative.

The boy gave a history of stiffness and swelling of the right knee joint in June, 1932. The following December, swollen nodes in the left groin were noted. In January, 1933, a fever developed, and the patient was in bed until the time of his admission to the hospital. The interstitial keratitis developed in February. Since February 14, the patient has received six injections of old arsphenamine, totaling 1.9 Gm., and eleven injections of 2 cc. each of soluble bismuth. There has been improvement in the condition of the eyes and knee joints, and it is the consensus that there has been a diminution in the size of the mass in the pelvis.

DISCUSSION

DR. F. D. WEIDMAN: In cases like this presenting extensive involvement of the lymph nodes, studies of the blood are important. We should realize how rapidly hematology has advanced and how complicated the subject has become. Dermatologists should take advantage of the more complete hemograms, including the Schilling count, as well as of studies of biopsy specimens and material from the bone marrow. Such conditions as aleukemic leukemia and lymphosarcoma have been known for a long time, but of late such a refinement in the pathologic process in the lymphatic system as aleukemic reticulosis has been achieved. The possibilities of such essentially lymphatic changes extending into the skin should be kept in mind.

DR. A. D. KING: The interstitial keratitis developed after the institution of bismuth therapy.

DR. D. M. PILLSBURY: It was Dr. Stokes' belief that possibly this was an example of the condition described by Vignolo Luttati, in which a combined syphilitic and tuberculous infection occurs with enormous enlargement of the lymph nodes.

Dr. R. L. Gilman: It will be worth while to test this boy with the Frei antigen.

A Case for Diagnosis (Tuberculosis?). Presented by Dr. A. D. King for Dr. John H. Stokes.

A white American student, aged 14, presents three granulomas on the dorsum of the right foot near the base of the toes. The older process consists of a coin-sized cicatricial area just back of the second and third toes, with evidence of chronic inflammation of parts of the border. There are two satellite granulomas nearby, extending in a straight line backward and outward from the original sites. Lymphadenopathy was not discovered anywhere on this extremity. A roentgenogram taken some time ago showed no changes in the bones. The Wassermann test of the blood was negative. The biopsy was suggestive of tuberculosis.

The onset dates back twelve years, when an inflammatory nodule appeared at the site of the scar. This slowly increased in size, leaving contractile scar tissue in the areas which had healed. The satellite nodules are of more recent development. Therapy has been confined to local applications.

DISCUSSION

Dr. F. D. Weidman: I was struck by a somewhat linear arrangement of the lesions and by the duskiness and cold feet. The latter suggest a tuberculous factor. I wonder whether the condition could be regarded as Wende's nodular tuberculosis of the hypoderm. I can understand that if the disease began below an interdigital position it would be located at places other than the classic position for such tuberculosis on the leg.

Dr. V. C. Garner: If we must classify the condition, I suggest tuberculosis colliquativa, in view of the negative roentgen studies for pathologic changes in the bones.

Dr. S. S. Greenbaum: I suggest a fixed dressing for a month or six weeks, and a subsequent report.

Exfoliative Dermatitis. Presented by Dr. H. Beerman.

C. W., a white man, aged 49, an executive in an ice company, presents a marked generalized erythema with profuse scaling on the face, arms, neck and forearms. The lower extremities are cyanotic, almost tending to purpura. There is marked edema of the face. The tongue is dry, red and shiny; the throat is covered with a thick exudate. There are scattered rhonchi in the chest. The blood pressure was 102 systolic and 60 diastolic; the temperature was 101.4 F.

On admission to the hospital, the blood count showed 29,000 leukocytes with 9 per cent eosinophils. The blood urea nitrogen was 27 mg. The urine was normal. Repeated tests of the blood showed from 13,200 to 27,000 leukocytes, with from 2 to 8 per cent eosinophils. The Wassermann test of the blood was negative.

The patient said that in October, 1932, he had an attack of cutaneous lesions which were not associated with fever, chills or sweats. In January, 1933, he complained of abdominal pain. On March 29, he complained of a generalized pruritic eruption with fever; this was associated with sore throat. After several days the eruption seemed to subside but suddenly flared up, and on April 5 he presented what appeared to be a generalized toxic erythema with a probable septic focus in the throat. On April 7, 8 and 9, he had marked diarrhea and a temperature ranging from 103 to 105 F. The leukocyte count at that time was 8,000. Shortly before admission to the hospital on April 10, scaling of the body began. There was no history of the taking of arsphenamine or other contact with arsenical preparations, nor was there a history of the ingestion of other drugs, such as phenolphthalein. He has had no psoriasis.

DISCUSSION

DR. H. BEERMAN: The medical men are puzzled. They cannot find a cause for the high fever, except the dermatologic condition. The condition of the throat would not account for a temperature of 105 F.

DR. F. D. WEIDMAN: Theoretically, a skin that is in a severely exfoliative and congestive state should entail disturbance of heat regulation. Most of these patients complain of chilliness. This one is different in that respect. I wonder whether the condition is going to develop into granuloma fungoides.

DR. W. O. ROOP: There are so many ways in which arsenic is used in the trades these days. A few years ago I saw a paper-hanger in whom severe exfoliative dermatitis developed. He had been hanging a great deal of green paper, and we presume that the green paper gets its color from the large amount of arsenic in it. I think that we should determine carefully the arsenic background in these cases. I should suggest, from an empirical standpoint, that sodium thiosulphate be administered intravenously.

SUBSEQUENT REPORT.—The patient's skin and general condition became normal, but there was a rather sudden recurrence of the exfoliative features and fever, which were again subsiding.

PHENOLPHTHALEIN ERUPTION. Presented by DR. H. BEERMAN.

An Italian youth, aged 19, presents an intense erythema associated with a rather bluish hyperpigmentation. The process is concentrated on the extremities and around the buttocks. There are eroded lesions in the mouth and on the genitalia. The latter are markedly swollen. The nails show evidences of the formation of new nails underneath the old. There is a generalized tender lymphadenopathy except in the cervical region. The joints are sore and painful. On examination, the heart presented a systolic murmur, and his diastolic blood pressure could not be determined.

While the patient was in the hospital his blood count showed 35,000 leukocytes with 1 per cent eosinophils. The urine was normal. Subsequent blood counts showed 14,000 leukocytes, with from 1 to 12 per cent eosinophils. Several serologic tests gave conflicting results, negative and positive. Smears from the mouth showed a few spirochetes (Vincent's).

The patient came to the University Hospital on March 19, 1933, complaining of a generalized eruption of the skin and itching. He said that he had been well until in 1929, when sore mouth developed, which healed in two and one-half weeks. In 1930, he had a recurrence associated with the eruption of the skin and the itching. Since then he has had two other attacks, the last in January, 1933. During the last two attacks he was confined to hospitals. On the third attack, on April 6, a suggestion of secondary syphilis was entertained, but the Wassermann tests of the blood and the spinal fluid were negative. A smear from the gums was negative for Vincent's organism. The final diagnosis was balanoposthitis. The fourth attack was diagnosed as erythema multiforme. Prior to the patient's admission to the hospital, he received thirty injections of neoarsphenamine from a private physician. While in the hospital he presented a profuse macular eruption over the entire body. On the day of admission he had a temperature of 103 F., which gradually fell. The eruption involuted after about eight days, but this process was preceded by marked exfoliation of the skin, leaving the hyperpigmented lesions which are now present.

The drug which the patient took was called "Italian Effervescent Salts." He is exhibited primarily to show the elusive nature of phenolphthalein eruptions, as well as the complicating factor of high fever in this particular instance.

There was an exhibit of a few laxatives containing phenolphthalein.

DISCUSSION

DR. F. D. WEIDMAN: In principle, phenolphthalein dermatitis is erythema multiforme perstans; i. e., it is connected with internal processes. It may be that

the constitutional symptoms in this patient are caused by the fact that the lesions are also occurring in the internal organs, perhaps in the central nervous system, which occurrence would account for the rise in temperature. Edema of the larynx, for example (and probably of other internal parts), occurs in urticaria.

DR. H. BEERMAN: When the patient first entered the hospital, we thought that he might have something to account for the fever, but the medical men could not find anything.

A CASE FOR DIAGNOSIS. Presented by DR. H. BEERMAN.

On March 30, 1933, a colored housewife, aged 33, presented a profuse eruption of black, pigmented spots, involving the trunk and extremities, with occasional lesions on the face. She was four months pregnant. The serologic tests gave negative results, but the patient was under treatment for syphilis.

The patient was first seen on June 5, 1931, with a condition diagnosed as latent syphilis. She was given regular treatment with bismuth and neoarsphenamine. During the course of treatment she became pregnant, and coincident with pregnancy, in 1932, generalized hyperpigmented lesions began to develop. At the termination of pregnancy, the lesions became less intense. About four months ago she again became pregnant, with a subsequent flare-up in the intensity of the hyperpigmented lesions. There was also associated pruritus. There is no history of the ingestion of drugs.

DISCUSSION

DR. F. D. WEIDMAN: Most of us thought of a phenolphthalein eruption.

DR. S. S. GREENBAUM: The patient has been receiving injections of neoarsphenamine. I believe that she has a fixed eruption due to arsenic. The injections were discontinued after she had her last baby; when she became pregnant, she again received injections.

DR. F. D. WEIDMAN: I have seen large patches of pigmentation, arranged symmetrically, too, in a Negress who had a uterine fibroid irradiated. There is another instance in which the female reproductive parts were stimulated.

DR. H. BEERMAN: In reference to Dr. Greenbaum's remarks, there was no effect of the treatment with neoarsphenamine and bismuth on the hyperpigmented lesions when the patient was not pregnant, but now, with pregnancy, the lesions have become pruritic, as they did during the previous pregnancy.

DR. S. S. GREENBAUM: The pigmentation can be disregarded. Pigmentation occurs in the presence of inflammatory lesions. The patient has definite pigmented lesions. I still believe that the condition is a fixed eruption due to arsenic in addition to some toxic underlying factor.

DR. F. D. WEIDMAN: I suggest an Aschheim-Zondek test. If the result is positive, it would mean nothing in regard to the dermatosis, but, if negative, it would indicate an upset of the endocrine balance, on which the Aschheim-Zondek test depends.

A CASE FOR DIAGNOSIS (ACRODERMATITIS CHRONICA ATROPHICANS?). Presented by DR. C. S. WRIGHT.

On March 1, 1933, I. D., a white woman, aged 51, complained of coldness and numbness of the legs. Examination revealed a cyanotic discoloration of the outer side of the left leg, extending from the knee to the ankle. The left foot was of normal color. The right foot presented a purplish, violaceous cyanosis of the right ankle and right knee. The right leg, between the knee and ankle, showed very little discoloration. Both thighs showed a mild, reticulated discoloration suggestive of cutis marmorata. The patient stated that the discoloration began about three years ago, with reddish patches on the dorsum of the right foot. She has recently received treatment for an old gonorrheal bartholinitis and also for latent syphilis. She complains of hot flushes and headaches, and flows profusely at her menstrual periods, which have become irregular.

The Wassermann reaction of the blood was 4 plus. The spinal fluid gave a negative Wassermann test and a colloidal gold test. There was no increase in globulin and only 1 or 2 cells per field. Oscillometric tests showed normal pulsation readings below both knees and at both ankles. Examination of the cardiovascular system gave negative results, although the descending aorta was somewhat widened. It is suggested that the patient's condition is one of faulty vasomotor mechanism.

DISCUSSION

DR. F. D. WEIDMAN: One arm shows livedo reticularis, which is difficult to relate to the more diffuse pigmentation of the lower extremities. I believe that there is a neurologic basis for the dermatitis because the skin of the lower extremities is atrophic. However, I should not be willing to classify the condition outright as acrodermatitis chronica atrophicans.

DR. E. F. CORSON: I thought that the condition was acrodermatitis chronica atrophicans. There were grossly atrophic skin, permanently dilated vessels and more or less severity in the lower portion of the leg, diminishing farther up toward the knee. It had practically reached the level of the upper third of the tibia, as I recall.

DR. T. BUTTERWORTH: I suggest a diagnosis of erythromelalgia. The condition began peripherally and has extended upward. It is worse when the foot hangs down. When the patient walks, a bluish tinge appears, and she has a drawing pain in the feet.

Books Received

An Introduction to Dermatology. By Richard L. Sutton and Richard L. Sutton, Jr. Pp. 566, with 190 illustrations. St. Louis: C. V. Mosby Company, 1933.

The History and Epidemiology of Syphilis. By William Allen Pusey. Price, $2. Pp. 113, with 37 illustrations. Springfield, Ill.: Charles C. Thomas, 1933.

CORRECTIONS

In the transactions of the February 15 meeting of the Chicago Dermatological Society, which appeared in the September issue of the Archives (**28**:436, 1933), an error occurred in Dr. Ormsby's discussion of the paper by Dr. Senear and Dr. Caro, entitled, "Mycosis Fungoides," on page 447. The word "nonsyphilitic" in the eighth line of the discussion should have been "nonspecific."

In the article by C. W. Emmons, entitled, "Fungicidal Action of Some Common Disinfectants on Two Dermatophytes," which appeared in the July issue of the Archives (**28**:15, 1933), the phenol coefficient of phenyl-mercuric-nitrate as shown in the table on page 18 should appear as 140 instead of 14.

Directory of Dermatologic Societies *

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

Alberic Marin, President, Drummond Medical Bldg., Montreal.
Antonio Sabetta, Secretary-Treasurer, 3435 St. Denis St., Montreal.
Place: Hamilton, Ontario. Time: 1934.

Royal Society of Medicine, Section of Dermatology

A. M. H. Gray, President, 30 New Cavendish St., W. 1, London.
W. N. Goldsmith, Secretary, 6, Upper Wimpole St., W. 1, London.

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

C. Guy Lane, Chairman, 416 Marlboro St., Boston.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Cleveland. Time: June 11-15, 1934.

American Dermatological Association

Fred Wise, President, 200 W. 59th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Harry M. Robinson, President, 106 E. Chase St., Baltimore.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Emmett C. Troxell, President, 74 W. Adams St., Detroit.
William G. Saunders, Secretary, 9203 Grand River Ave., Detroit.
Place: Pittsburgh. Time: 1933.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City, Iowa.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

New England Dermatological Society

Rudolph Jacoby, President, 270 Commonwealth Ave., Boston.
J. Harper Blaisdell, Secretary, 5 Bay State Road, Boston.
Place: Boston. Time: April 11, 1934.

Southern Medical Association, Section on Dermatology and Syphilology

Andrew L. Glaze, Chairman, 1928 First Avenue, Birmingham, Ala.
Dudley C. Smith, Secretary, University, Va.
Place: Richmond, Va. Time: November 14-17, 1933.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
Elmo D. French, Secretary, 602 Huntington Bldg., Miami.
Place: Jacksonville. Time: July 2, 1934.

Louisiana Dermatological Society

J. A. Devron, President, 150 Baronne St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 912 Pere Marquette Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Fisher, Chairman, 264 Genesee St., Utica.
Frank Combes, Secretary, 80 W. 40th St., New York.

Medical Society of the State of Pennsylvania Section on Dermatology

Herbert J. Smith, President, 3303 N. 17th St., Philadelphia.
Robert L. Gilman, Secretary, 1930 Chestnut St., Philadelphia.

Michigan State Medical Society, Section on Dermatology and Syphilology

Robert C. Jamieson, Chairman, 1551 Woodward Ave., Detroit.
A. R. Woodburne, Secretary, Grand Rapids Clinic, Grand Rapids.
Place: Battle Creek. Time: September, 1934.

Minnesota Dermatological Society

E. Z. Shapiro, President, 14 W. Superior St., Duluth.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma Dermatological Association

W. A. Showman, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 505 Osler Bldg., Oklahoma City.

Texas Dermatological Society

Everett C. Fox, President, 1719 Pacific Ave., Dallas.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Houston. Time: Fall, 1933.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Samuel Feldman, Chairman, 1955 Grand Concourse, New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Louis J. Frank, President, 1367 Eastern Parkway, Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo Dermatological Society

Joseph Brumberg, President, 528 Delaware Ave., Buffalo.
William F. Hoover, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Max Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Harry L. Claassen, President, Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

S. Littman, President, 10515 Carnegie Ave., Cleveland.
H. G. Miskjian, Secretary, 856 Rose Bldg., Cleveland.

Detroit Dermatological Society

H. L. Keim, President, 10 Witherell St., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

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